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(54) **CROSS-SPECIES-SPECIFIC PSMA X CD3 BISPECIFIC SINGLE CHAIN ANTIBODY**

(57) The present invention relates to a bispecific single chain antibody molecule comprising a first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 epsilon chain, wherein the epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID NOs. 2, 4, 6, and 8, and a second binding domain capable of binding to prostate-specific membrane antigen (PSMA). The invention

also provides nucleic acids encoding said bispecific single chain antibody molecule as well as vectors and host cells and a process for its production. The invention further relates to pharmaceutical compositions comprising said bispecific single chain antibody molecule and medical uses of said bispecific single chain antibody molecule.

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Description

[0001] The present invention relates to a bispecific single chain antibody molecule comprising a first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 epsilon chain, wherein the epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID NOs. 2, 4, 6, and 8, and a second binding domain capable of binding to prostate-specific membrane antigen (PSMA). The invention also provides nucleic acids encoding said bispecific single chain antibody molecule as well as vectors and host cells and a process for its production. The invention further relates to pharmaceutical compositions comprising said bispecific single chain antibody molecule and medical uses of said bispecific single chain antibody molecule.

[0002] T cell recognition is mediated by clonotypically distributed alpha beta and gamma delta T cell receptors (TcR) that interact with the peptide-loaded molecules of the peptide MHC (pMHC) (Davis & Bjorkman, *Nature* 334 (1988), 395-402). The antigen-specific chains of the TcR do not possess signalling domains but instead are coupled to the conserved multisubunit signaling apparatus CD3 (Call, *Cell* 111 (2002), 967-979, Alarcon, *Immunol. Rev.* 191 (2003), 38-46, Malissen *Immunol. Rev.* 191 (2003), 7-27). The mechanism by which TcR ligation is directly communicated to the signalling apparatus remains a fundamental question in T cell biology (Alarcon, loc. cit.; Davis, *Cell* 110 (2002), 285-287). It seems clear that sustained T cell responses involve coreceptor engagement, TcR oligomerization, and a higher order arrangement of TcR-pMHC complexes in the immunological synapse (Davis & van der Merwe, *Curr. Biol.* 11 (2001), R289-R291, Davis, *Nat. Immunol.* 4 (2003), 217-224). However very early TcR signalling occurs in the absence of these events and may involve a ligand-induced conformational change in CD3 epsilon (Alarcon, loc. cit., Davis (2002), loc. cit., Gil, *J. Biol. Chem.* 276 (2001), 11174-11179, Gil, *Cell* 109 (2002), 901-912). The epsilon, gamma, delta and zeta subunits of the signaling complex associate with each other to form a CD3 epsilon-gamma heterodimer, a CD3 epsilon-delta heterodimer, and a CD3 zeta-zeta homodimer (Call, loc. cit.). Various studies have revealed that the CD3 molecules are important for the proper cell surface expression of the alpha beta TcR and normal T cell development (Berkhout, *J. Biol. Chem.* 263 (1988), 8528-8536, Wang, *J. Exp. Med.* 188 (1998), 1375-1380, Kappes, *Curr. Opin. Immunol.* 7 (1995), 441-447). The solution structure of the ectodomain fragments of the mouse CD3 epsilon gamma heterodimer showed that the epsilon gamma subunits are both C2-set Ig domains that interact with each other to form an unusual side-to-side dimer configuration (Sun, *Cell* 105 (2001), 913-923). Although the cysteine-rich stalk appears to play an important role in driving CD3 dimerization (Su, loc. cit., Borroto, *J. Biol. Chem.* 273 (1998), 12807-12816), interaction by means of the extracellular domains of CD3 epsilon and CD3 gamma is sufficient for assembly of these proteins with TcR beta (Manolios, *Eur. J. Immunol.* 24 (1994), 84-92, Manolios & Li, *Immunol. Cell Biol.* 73 (1995), 532-536). Although still controversial, the dominant stoichiometry of the TcR most likely comprises one alpha beta TcR, one CD3 epsilon gamma heterodimer, one CD3 epsilon delta heterodimer and one CD3 zeta zeta homodimer (Call, loc. cit.). Given the central role of the human CD3 epsilon gamma heterodimer in the immune response, the crystal structure of this complex bound to the therapeutic antibody OKT3 has recently been elucidated (Kjer-Nielsen, *PNAS* 101, (2004), 7675-7680).

[0003] A number of therapeutic strategies modulate T cell immunity by targeting TcR signaling, particularly the anti-human CD3 monoclonal antibodies (mAbs) that are widely used clinically in immunosuppressive regimes. The CD3-specific mouse mAb OKT3 was the first mAb licensed for use in humans (Sgro, *Toxicology* 105 (1995), 23-29) and is widely used clinically as an immunosuppressive agent in transplantation (Chatenoud, *Clin. Transplant* 7 (1993), 422-430, Chatenoud, *Nat. Rev. Immunol.* 3 (2003), 123-132, Kumar, *Transplant. Proc.* 30 (1998), 1351-1352), type 1 diabetes (Chatenoud (2003), loc. cit.), and psoriasis (Utset, *J. Rheumatol.* 29 (2002), 1907-1913). Moreover, anti-CD3 mAbs can induce partial T cell signalling and clonal anergy (Smith, *J. Exp. Med.* 185 (1997), 1413-1422). OKT3 has been described in the literature as a potent T cell mitogen (Van Wauve, *J. Immunol.* 124 (1980), 2708-18) as well as a potent T cell killer (Wong, *Transplantation* 50 (1990), 683-9). OKT3 exhibits both of these activities in a time-dependent fashion; following early activation of T cells leading to cytokine release, upon further administration OKT3 later blocks all known T cell functions. It is due to this later blocking of T cell function that OKT3 has found such wide application as an immunosuppressant in therapy regimens for reduction or even abolition of allograft tissue rejection.

[0004] OKT3 reverses allograft tissue rejection most probably by blocking the function of all T cells, which play a major role in acute rejection. OKT3 reacts with and blocks the function of the CD3 complex in the membrane of human T cells, which is associated with the antigen recognition structure of T cells (TCR) and is essential for signal transduction. Which subunit of the TCR/CD3 is bound by OKT3 has been the subject of multiple studies. Though some evidence has pointed to a specificity of OKT3 for the epsilon-subunit of the TCR/CD3 complex (Tunnacliffe, *Int. Immunol.* 1 (1989), 546-50; Kjer-Nielsen, *PNAS* 101, (2004), 7675-7680). Further evidence has shown that OKT3 binding of the TCR/CD3 complex requires other subunits of this complex to be present (Salmeron, *J. Immunol.* 147 (1991), 3047-52).

[0005] Other well known antibodies specific for the CD3 molecule are listed in Tunnacliffe, *Int. Immunol.* 1 (1989), 546-50. As indicated above, such CD3 specific antibodies are able to induce various T cell responses such as lymphokine production (Von Wussow, *J. Immunol.* 127 (1981), 1197; Palacios, *J. Immunol.* 128 (1982), 337), proliferation (Van Wauve, *J. Immunol.* 124 (1980), 2708-18) and suppressor-T cell induction (Kunicka, in "Lymphocyte Typing II" 1 (1986),

223). That is, depending on the experimental conditions, CD3 specific monoclonal antibody can either inhibit or induce cytotoxicity (Leewenberg, J. Immunol. 134 (1985), 3770; Phillips, J. Immunol. 136 (1986) 1579; Platsoucas, Proc. Natl. Acad. Sci. USA 78 (1981), 4500; Itoh, Cell. Immunol. 108 (1987), 283-96; Mentzer, J. Immunol. 135 (1985), 34; Landegren, J. Exp. Med. 155 (1982), 1579; Choi (2001), Eur. J. Immunol. 31, 94-106; Xu (2000), Cell Immunol. 200, 16-26; Kimball (1995), Transpl. Immunol. 3, 212-221).

[0006] Although many of the CD3 antibodies described in the art have been reported to recognize the CD3 epsilon subunit of the CD3 complex, most of them bind in fact to conformational epitopes and, thus, only recognize CD3 epsilon in the native context of the TCR. Conformational epitopes are characterized by the presence of two or more discrete amino acid residues which are separated in the primary sequence, but come together on the surface of the molecule when the polypeptide folds into the native protein/antigen (Sela, (1969) Science 166, 1365 and Laver, (1990) Cell 61, 553-6). The conformational epitopes bound by CD3 epsilon antibodies described in the art may be separated in two groups. In the major group, said epitopes are being formed by two CD3 subunits, e.g. of the CD3 epsilon chain and the CD3 gamma or CD3 delta chain. For example, it has been found in several studies that the most widely used CD3 epsilon monoclonal antibodies OKT3, WT31, UCHT1, 7D6 and Leu-4 did not bind to cells singly transfected with the CD3-epsilon chain. However, these antibodies stained cells doubly transfected with a combination of CD3 epsilon plus either CD3 gamma or CD3 delta (Tunnacliffe, loc. cit.; Law, Int. Immunol. 14 (2002), 389-400; Salmeron, J. Immunol. 147 (1991), 3047-52; Coulie, Eur. J. Immunol. 21 (1991), 1703-9). In a second smaller group, the conformational epitope is being formed within the CD3 epsilon subunit itself. A member of this group is for instance mAb APA 1/1 which has been raised against denatured CD3 epsilon (Risueno, Blood 106 (2005), 601-8). Taken together, most of the CD3 epsilon antibodies described in the art recognize conformational epitopes located on two or more subunits of CD3. The discrete amino acid residues forming the three-dimensional structure of these epitopes may hereby be located either on the CD3 epsilon subunit itself or on the CD3 epsilon subunit and other CD3 subunits such as CD3 gamma or CD3 delta.

[0007] Another problem with respect to CD3 antibodies is that many CD3 antibodies have been found to be species-specific. Anti-CD3 monoclonal antibodies - as holds true generally for any other monoclonal antibodies - function by way of highly specific recognition of their target molecules. They recognize only a single site, or epitope, on their target CD3 molecule. For example, one of the most widely used and best characterized monoclonal antibodies specific for the CD3 complex is OKT-3. This antibody reacts with chimpanzee CD3 but not with the CD3 homolog of other primates, such as macaques, or with dog CD3 (Sandusky et al., J. Med. Primatol. 15 (1986), 441-451). Similarly, WO2005/118635 or WO2007/033230 describe human monoclonal CD3 epsilon antibodies which react with human CD3 epsilon but not with CD3 epsilon of mouse, rat, rabbit or non-chimpanzee primates such as rhesus monkey, cynomolgus monkey or baboon monkey. The anti-CD3 monoclonal antibody UCHT-1 is also reactive with CD3 from chimpanzee but not with CD3 from macaques (own data). On the other hand, there are also examples of monoclonal antibodies, which recognize macaque antigens, but not their human counterparts. One example of this group is monoclonal antibody FN-18 directed to CD3 from macaques (Uda et al., J. Med. Primatol. 30 (2001), 141-147). Interestingly, it has been found that peripheral lymphocytes from about 12% of cynomolgus monkeys lacked reactivity with anti-rhesus monkey CD3 monoclonal antibody (FN-18) due to a polymorphism of the CD3 antigen in macaques. Uda et al. described a substitution of two amino acids in the CD3 sequence of cynomolgus monkeys, which are not reactive with FN-18 antibodies, as compared to CD3 derived from animals, which are reactive with FN-18 antibodies (Uda et al., J Med Primatol. 32 (2003), 105-10; Uda et al., J Med Primatol. 33 (2004), 34-7).

[0008] The discriminatory ability, i.e. the species specificity, inherent not only to CD3 monoclonal antibodies (and fragments thereof), but to monoclonal antibodies in general, is a significant impediment to their development as therapeutic agents for the treatment of human diseases. In order to obtain market approval any new candidate medication must pass through rigorous testing. This testing can be subdivided into preclinical and clinical phases: Whereas the latter - further subdivided into the generally known clinical phases I, II and III - is performed in human patients, the former is performed in animals. The aim of pre-clinical testing is to prove that the drug candidate has the desired activity and most importantly is safe. Only when the safety in animals and possible effectiveness of the drug candidate has been established in preclinical testing this drug candidate will be approved for clinical testing in humans by the respective regulatory authority. Drug candidates can be tested for safety in animals in the following three ways, (i) in a relevant species, i.e. a species where the drug candidates can recognize the ortholog antigens, (ii) in a transgenic animal containing the human antigens and (iii) by use of a surrogate for the drug candidate that can bind the ortholog antigens present in the animal. Limitations of transgenic animals are that this technology is typically limited to rodents. Between rodents and man there are significant differences in the physiology and the safety results cannot be easily extrapolated to humans. The limitations of a surrogate for the drug candidate are the different composition of matter compared to the actual drug candidate and often the animals used are rodents with the limitation as discussed above. Therefore, preclinical data generated in rodents are of limited predictive power with respect to the drug candidate. The approach of choice for safety testing is the use of a relevant species, preferably a lower primate. The limitation now of monoclonal antibodies suitable for therapeutic intervention in man described in the art is that the relevant species are higher primates, in particular chimpanzees. Chimpanzees are considered as endangered species and due to their human-like nature, the use of such

animals for drug safety testing has been banned in Europe and is highly restricted elsewhere. CD3 has also been successfully used as a target for bispecific single chain antibodies in order to redirect cytotoxic T cells to pathological cells, resulting in the depletion of the diseased cells from the respective organism (WO 99/54440; WO 04/106380). For example, Bargou et al. (Science 321 (2008):974-7) have recently reported on the clinical activity of a CD19xCD3 bispecific antibody construct called blinatumomab, which has the potential to engage all cytotoxic T cells in human patients for lysis of cancer cells. Doses as low as 0.005 milligrams per square meter per day in non-Hodgkin's lymphoma patients led to an elimination of target cells in blood. Partial and complete tumor regressions were first observed at a dose level of 0.015 milligrams, and all seven patients treated at a dose level of 0.06 milligrams experienced a tumor regression. Blinatumomab also led to clearance of tumor cells from bone marrow and liver. Though this study established clinical proof of concept for the therapeutic potency of the bispecific single chain antibody format in treating blood-cell derived cancer, there is still need for successful concepts for therapies of other cancer types.

[0009] In 2008, an estimated 186,320 men will be newly diagnosed with prostate cancer in the United States and about 28,660 men will die from the disease. The most recent report available on cancer mortality shows that, in 2004, the overall death rate from prostate cancer among American men was 25 per 100,000. In the late 1980s, the widespread adoption of the prostate-specific antigen (PSA) test represented a major improvement in the management of prostate cancer. This test measures the amount of PSA protein in the blood, which is often elevated in patients with prostate cancer. In 1986, the U.S. Food and Drug Administration approved the use of the PSA test to monitor patients with prostate cancer and, in 1994, additionally approved its use as a screening test for this disease. Due to the widespread implementation of PSA testing in the United States, approximately 90 percent of all prostate cancers are currently diagnosed at an early stage, and, consequently, men are surviving longer after diagnosis. However, the results of two ongoing clinical trials, the NCI-sponsored Prostate, Lung, Colorectal, and Ovarian (PLCO) screening trial and the European Study of Screening for Prostate Cancer (ERSPC) will be needed to determine whether PSA screening actually saves lives. Ongoing clinical trials over the past 25 years have investigated the effectiveness of natural and synthetic compounds in the prevention of prostate cancer. For example, the Prostate Cancer Prevention Trial (PCPT), which enrolled nearly 19,000 healthy men, found that finasteride, a drug approved for the treatment of benign prostatic hyperplasia (BPH), which is a noncancerous enlargement of the prostate, reduced the risk of developing prostate cancer by 25 percent. Another trial, the Selenium and Vitamin E Cancer Prevention Trial (SELECT), is studying more than 35,000 men to determine whether daily supplements of selenium and vitamin E can reduce the incidence of prostate cancer in healthy men. Other prostate cancer prevention trials are currently evaluating the protective potential of multivitamins, vitamins C and D, soy, green tea, and lycopene, which is a natural compound found in tomatoes. One study, reported in 2005, showed that specific genes were fused in 60 to 80 percent of the prostate tumors analyzed. This study represents the first observation of non-random gene rearrangements in prostate cancer. This genetic alteration may eventually be used as a biomarker to aid in the diagnosis and, possibly, treatment of this disease. Other studies have shown that genetic variations in a specific region of chromosome 8 can increase a man's risk of developing prostate cancer. These genetic variations account for approximately 25 percent of the prostate cancers that occur in white men. They are the first validated genetic variants that increase the risk of developing prostate cancer and may help scientists better understand the genetic causes of this disease. There is also ongoing research that examines how proteins circulating in a patient's blood can be used to improve the diagnosis of prostate and other cancers. In 2005, scientists identified a group of specific proteins that are produced by a patient's immune system in response to prostate tumors. These proteins, a type of autoantibody, were able to detect the presence of prostate cancer cells in blood specimens with greater than 90 percent accuracy. When used in combination with PSA, these and other blood proteins may eventually be used to reduce the number of false-positive results obtained with PSA testing alone and, therefore, reduce the large number of unnecessary prostate biopsies that are performed each year due to false-positive PSA test results.

[0010] Apart from PSA, several other markers for prostate cancer have been identified, including e.g. the six-transmembrane epithelial antigen of the prostate (STEAP) (Hubert et al., PNAS 96 (1999), 14523-14528), the prostate stem cell antigen (PSCA) (Reiter et al., Proc. Nat. Acad. Sci. 95: 1735-1740, 1998) and the prostate-specific membrane antigen (PSMA; PSM) (Israeli et al., Cancer Res. 53 (1993). PSMA was originally defined by the monoclonal antibody (MAb) 7E11 derived from immunization with a partially purified membrane preparation from the lymph node prostatic adenocarcinoma (LNCaP) cell line (Horoszewicz et al., Anticancer Res. 7 (1987), 927-35). A 2.65-kb cDNA fragment encoding the PSMA protein was cloned and subsequently mapped to chromosome 11 p11.2 (Israeli et al., loc. cit.; O'Keefe et al., Biochem. Biophys. Acta 1443 (1998), 113-127). Initial analysis of PSMA demonstrated widespread expression within the cells of the prostatic secretory epithelium. Immunohistochemical staining demonstrated that PSMA was absent to moderately expressed in hyperplastic and benign tissues, while malignant tissues stained with the greatest intensity (Horoszewicz et al., loc. cit.). Subsequent investigations have recapitulated these results and evinced PSMA expression as a universal feature in practically every prostatic tissue examined to date. These reports further demonstrate that expression of PSMA increases precipitously proportional to tumor aggressiveness (Burger et al., Int. J. Cancer 100 (2002), 228-237; Chang et al., Cancer Res. 59 (1999), 3192-98; Chang et al., Urology 57 (2001), 1179-83), Kawakami and Nakayama, Cancer Res. 57 (1997), 2321-24; Liu et al., Cancer Res. 57 (1997), 3629-34; Lopes et al., Cancer Res.

50 (1990), 6423-29; Silver et al., Clin. Cancer Res. 9 (2003), 6357-62; Sweat et al., Urology 52 (1998), 637-40; Troyer et al., Int. J. Cancer 62 (1995), 552-558; Wright et al., Urology 48 (1996), 326-334). Consistent with the correlation between PSMA expression and tumor stage, increased levels of PSMA are associated with androgen-independent prostate cancer (PCa). Analysis of tissue samples from patients with prostate cancer has demonstrated elevated PSMA levels after physical castration or androgen-deprivation therapy. Unlike expression of prostate specific antigen, which is downregulated after androgen ablation, PSMA expression is significantly increased in both primary and metastatic tumor specimens (Kawakami et al., Wright et al., loc. cit.). Consistent with the elevated expression in androgen-independent tumors, PSMA transcription is also known to be downregulated by steroids, and administration of testosterone mediates a dramatic reduction in PSMA protein and mRNA levels (Israeli et al., Cancer Res. 54 (1994), 1807-11; Wright et al., loc. cit.). PSMA is also highly expressed in secondary prostatic tumors and occult metastatic disease. Immunohistochemical analysis has revealed relatively intense and homogeneous expression of PSMA within metastatic lesions localized to lymph nodes, bone, soft tissue, and lungs compared with benign prostatic tissues (Chang et al. (2001), loc. cit.; Murphy et al., Cancer 78 (1996), 809-818; Sweat et al., loc. cit.). Some reports have also indicated limited PSMA expression in extraprostatic tissues, including a subset of renal proximal tubules, some cells of the intestinal brush-border membrane, and rare cells in the colonic crypts (Chang et al. (1999), Horoszewicz et al., Israeli et al. (1994), Lopes et al., Troyer et al., loc. cit.). However, the levels of PSMA in these tissues are generally two to three orders of magnitude less than those observed in the prostate (Sokoloff et al., Prostate 43 (2000), 150-157). PSMA is also expressed in the tumor-associated neovasculature of most solid cancers examined yet is absent in the normal vascular endothelium (Chang et al. (1999), Liu et al., Silver et al., loc. cit.). Although the significance of PSMA expression within the vasculature is unknown, the specificity for tumor-associated endothelium makes PSMA a potential target for the treatment of many forms of malignancy.

[0011] Though there has been put much effort in identifying novel targets for therapeutic approaches for cancer, cancer is yet one of the most frequently diagnosed diseases. In light of this, there is still need for effective treatments for cancer.

[0012] The present invention provides for a bispecific single chain antibody molecule comprising a first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 ϵ (epsilon) chain, wherein the epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID NOs. 2, 4, 6, and 8; and a second binding domain capable of binding to prostate-specific membrane antigen (PSMA).

[0013] Though T cell-engaging bispecific single chain antibodies described in the art have great therapeutic potential for the treatment of malignant diseases, most of these bispecific molecules are limited in that they are species specific and recognize only human antigen, and - due to genetic similarity - likely the chimpanzee counterpart. The advantage of the present invention is the provision of a bispecific single chain antibody comprising a binding domain exhibiting cross-species specificity to human and non-chimpanzee primate of the CD3 epsilon chain.

[0014] In the present invention, an N-terminal 1-27 amino acid residue polypeptide fragment of the extracellular domain of CD3 epsilon was surprisingly identified which - in contrast to all other known epitopes of CD3 epsilon described in the art - maintains its three-dimensional structural integrity when taken out of its native environment in the CD3 complex (and optionally fused to a heterologous amino acid sequence such as EpCAM or an immunoglobulin Fc part). The present invention, therefore, provides for a bispecific single chain antibody molecule comprising a first binding domain capable of binding to an epitope of an N-terminal 1-27 amino acid residue polypeptide fragment of the extracellular domain of CD3 epsilon (which CD3 epsilon is, for example, taken out of its native environment and/or comprised by (presented on the surface of) a T-cell) of human and at least one non-chimpanzee primate CD3 epsilon chain, wherein the epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID NOs. 2, 4, 6, and 8; and a second binding domain capable of binding to prostate-specific membrane antigen (PSMA). Preferred non-chimpanzee primates are mentioned herein elsewhere. At least one (or a selection thereof or all) primate(s) selected from *Callithrix jacchus*; *Saguinus oedipus*, *Saimiri sciureus*, and *Macaca fascicularis* (either SEQ ID 1047 or 1048 or both), is (are) particularly preferred. *Macaca mulatta*, also known as Rhesus Monkey is also envisaged as another preferred primate. It is thus envisaged that antibodies of the invention bind to (are capable of binding to) the context independent epitope of an N-terminal 1-27 amino acid residue polypeptide fragment of the extracellular domain of CD3 epsilon of human and *Callithrix jacchus*, *Saguinus oedipus*, *Saimiri sciureus*, and *Macaca fascicularis* (either SEQ ID 1047 or 1048 or both), and optionally also to *Macaca mulatta*. A bispecific single chain antibody molecule comprising a first binding domain as defined herein can be obtained (is obtainable by) or can be manufactured in accordance with the protocol set out in the appended Examples (in particular Example 2). To this end, it is envisaged to (a) immunize mice with an N-terminal 1-27 amino acid residue polypeptide fragment of the extracellular domain of CD3 epsilon of human and/or *Saimiri sciureus*; (b) generation of an immune murine antibody scFv library; (c) identification of CD3 epsilon specific binders by testing the capability to bind to at least SEQ ID NOs. 2, 4, 6, and 8.

[0015] The context-independence of the CD3 epitope provided in this invention corresponds to the first 27 N-terminal amino acids of CD3 epsilon or functional fragments of this 27 amino acid stretch. The phrase "context-independent," as used herein in relation to the CD3 epitope means that binding of the herein described inventive binding molecules/antibody molecules does not lead to a change or modification of the conformation, sequence, or structure surrounding the antigenic

determinant or epitope. In contrast, the CD3 epitope recognized by a conventional CD3 binding molecule (e.g. as disclosed in WO 99/54440 or WO 04/106380) is localized on the CD3 epsilon chain C-terminally to the N-terminal 1-27 amino acids of the context-independent epitope, where it only takes the correct conformation if it is embedded within the rest of the epsilon chain and held in the right sterical position by heterodimerization of the epsilon chain with either the CD3 gamma or delta chain. Anti-CD3 binding domains as part of a PSMAxCD3 bispecific single chain molecule as provided herein and generated (and directed) against a context-independent CD3 epitope provide for a surprising clinical improvement with regard to T cell redistribution and, thus, a more favourable safety profile. Without being bound by theory, since the CD3 epitope is context-independent, forming an autonomous self-sufficient subdomain without much influence on the rest of the CD3 complex, the CD3 binding domain of the PSMAxCD3 bispecific single chain molecule provided herein induces less allosteric changes in CD3 conformation than the conventional CD3 binding molecules (like molecules provided in WO 99/54440 or WO 04/106380), which recognize context-dependent CD3 epitopes.

[0016] The context-independence of the CD3 epitope which is recognized by the CD3 binding domain of the PSMAxCD3 bispecific single chain antibody of the invention is associated with less or no T cell redistribution (T cell redistribution equates with an initial episode of drop and subsequent recovery of absolute T cell counts) during the starting phase of treatment with said PSMAxCD3 bispecific single chain antibody of the invention. This results in a better safety profile of the PSMAxCD3 bispecific single chain antibody of the invention compared to conventional CD3 binding molecules known in the art, which recognize context-dependent CD3 epitopes. Particularly, because T cell redistribution during the starting phase of treatment with CD3 binding molecules is a major risk factor for adverse events, like CNS adverse events, the PSMAxCD3 bispecific single chain antibody of the invention by recognizing a context-independent rather than a context-dependent CD3 epitope has a substantial safety advantage over the CD3 binding molecules known in the art. Patients with such CNS adverse events related to T cell redistribution during the starting phase of treatment with conventional CD3 binding molecules usually suffer from confusion and disorientation, in some cases also from urinary incontinence. Confusion is a change in mental status in which the patient is not able to think with his or her usual level of clarity. The patient usually has difficulties to concentrate and thinking is not only blurred and unclear but often significantly slowed down. Patients with CNS adverse events related to T cell redistribution during the starting phase of treatment with conventional CD3 binding molecules may also suffer from loss of memory. Frequently, the confusion leads to the loss of ability to recognize people, places, time or the date. Feelings of disorientation are common in confusion, and the decision-making ability is impaired. CNS adverse events related to T cell redistribution during the starting phase of treatment with conventional CD3 binding molecules may further comprise blurred speech and/or word finding difficulties. This disorder may impair both, the expression and understanding of language as well as reading and writing. Besides urinary incontinence, vertigo and dizziness may also accompany CNS adverse events related to T cell redistribution during the starting phase of treatment with conventional CD3 binding molecules in some patients.

[0017] The maintenance of the three-dimensional structure within the mentioned 27 amino acid N-terminal polypeptide fragment of CD3 epsilon can be used for the generation of, preferably human, binding domains which are capable of binding to the N-terminal CD3 epsilon polypeptide fragment *in vitro* and to the native (CD3 epsilon subunit of the) CD3 complex on T cells *in vivo* with the same binding affinity. These data strongly indicate that the N-terminal fragment as described herein forms a tertiary conformation, which is similar to its structure normally existing *in vivo*. A very sensitive test for the importance of the structural integrity of the amino acids 1-27 of the N-terminal polypeptide fragment of CD3 epsilon was performed. Individual amino acids of amino acids 1-27 of the N-terminal polypeptide fragment of CD3 epsilon were changed to alanine (alanine scanning) to test the sensitivity of the amino acids 1-27 of the N-terminal polypeptide fragment of CD3 epsilon for minor disruptions. The CD3 specific binding domains as part of the PSMAxCD3 bispecific single chain antibody of the invention were used to test for binding to the alanine-mutants of amino acids 1-27 of the N-terminal polypeptide fragment of CD3 epsilon (see appended Example 5). Individual exchanges of the first five amino acid residues at the very N-terminal end of the fragment and two of the amino acids at positions 23 and 25 of the amino acids 1-27 of the N-terminal polypeptide fragment of CD3 epsilon were critical for binding of the antibody molecules. The substitution of amino acid residues in the region of position 1-5 comprising the residues Q (Glutamine at position 1), D (Aspartic acid at position 2), G (Glycine at position 3), N (Asparagine at position 4), and E (Glutamic acid at position 5) to Alanine abolished binding of the, preferably human, PSMAxCD3 bispecific single chain antibody of the invention to said fragment. While, for at least some of the, preferably human, PSMAxCD3 bispecific single chain antibody of the invention, two amino acid residues at the C-terminus of the mentioned fragment T (Threonine at position 23) and I (Isoleucine at position 25) reduced the binding energy to the, preferably human, PSMAxCD3 bispecific single chain antibody of the invention.

[0018] Unexpectedly, it has been found that the thus isolated, preferably human, PSMAxCD3 bispecific single chain antibody of the invention not only recognizes the human N-terminal fragment of CD3 epsilon, but also the corresponding homologous fragments of CD3 epsilon of various primates, including New-World Monkeys (Marmoset, *Callithrix jacchus*; Saguinus oedipus; Saimiri sciureus) and Old-World Monkeys (*Macaca fascicularis*, also known as *Cynomolgus* Monkey; or *Macaca mulatta*, also known as Rhesus Monkey). Thus, multi-primate specificity of the PSMAxCD3 bispecific single chain antibody of the invention was detected. The following sequence analyses confirmed that human and primates

share a highly homologous sequence stretch at the N-terminus of the extracellular domain of CD3 epsilon.

[0019] The amino acid sequence of the aforementioned N-terminal fragments of CD3 epsilon are depicted in SEQ ID No. 2 (human), SEQ ID No. 4 (*Callithrix jacchus*); SEQ ID No. 6 (*Saguinus oedipus*); SEQ ID No. 8 (*Saimiri sciureus*); SEQ ID No. 1047 *QDGNEEMGSITQTPYQVSISGTTILTC* or SEQ ID No. 1048 *QDGNEEMGSITQTPYQVSISGTTVILT* (*Macaca fascicularis*, also known as *Cynomolgus Monkey*), and SEQ ID No. 1 049 *QDGNEEMGSITQTPYHVSISGTTVILT* (*Macaca mulatta*, also known as *Rhesus Monkey*).

[0020] The second binding domain of the PSMAxCD3 bispecific single chain antibody of the invention binds to the prostate-specific membrane antigen (PSMA). Preferably, the second binding domain of the PSMAxCD3 bispecific single chain antibody binds to the human PSMA or a non-chimpanzee primate PSMA; more preferred it binds to the human PSMA and a non-chimpanzee primate PSMA and therefore is cross-species specific; even more preferred to the human PSMA and the macaque PSMA (and therefore is cross-species specific as well). Particularly preferred, the macaque PSMA is the *Cynomolgus monkey* PSMA and/or the *Rhesus monkey* PSMA. However, it is not excluded from the scope of the present invention, that the second binding domain may also bind to PSMA homologs of other species, such as to the PSMA homolog in rodents.

[0021] Prostate cancer is the second most cancer in men. For 2008, it is estimated that 186,320 men will be newly diagnosed with prostate cancer in the United States and about 28,660 men will die from the disease. Prostate cancer risk is strongly related to age: very few cases are registered in men under 50 and three-quarters of cases occur in men over 65 years. The largest number of cases is diagnosed in those aged 70-74. Currently, the growth rate of the older population is significantly higher than that of the total population. By 2025-2030, projections indicate that the population over 60 will be growing 3.5 times as rapidly as the total population. The proportion of older persons is projected to more than double worldwide over the next half century, which means that a further increase in incidence of diagnosed prostate cancer has to be expected for the future. The highly restricted expression of PSMA and its upregulation in advanced stages and metastatic disease of prostate cancer as well as its role as neoantigen on tumor vasculature of many different types of other solid tumors qualifies PSMA as attractive target antigen for antibody-based cancer therapy. As shown in the following examples, the PSMAxCD3 bispecific single chain antibody of the invention provides an advantageous tool in order to kill PSMA-expressing human cancer cells, as exemplified by the human prostate cancer cell line LNCaP. In addition, the cytotoxic activity of the PSMAxCD3 bispecific single chain antibody of the invention is higher than the cytotoxic activity of antibodies described in the art. Since preferably both the CD3 and the PSMA binding domain of the PSMAxCD3 bispecific single chain antibody of the invention are cross-species specific, i.e. reactive with the human and non-chimpanzee primates antigens, it can be used for preclinical evaluation of safety, activity and/or pharmacokinetic profile of these binding domains in primates and - in the identical form - as drug in humans.

[0022] Advantageously, the present invention provides also PSMAxCD3 bispecific single chain antibodies comprising a second binding domain which binds both to the human PSMA and to the macaque PSMA homolog, i.e. the homolog of a non-chimpanzee primate. In a preferred embodiment, the bispecific single chain antibody thus comprises a second binding domain exhibiting cross-species specificity to the human and a non-chimpanzee primate PSMA. In this case, the identical bispecific single chain antibody molecule can be used both for preclinical evaluation of safety, activity and/or pharmacokinetic profile of these binding domains in primates and as drug in humans. Put in other words, the same molecule can be used in preclinical animal studies as well as in clinical studies in humans. This leads to highly comparable results and a much-increased predictive power of the animal studies compared to species-specific surrogate molecules. Since both the CD3 and the PSMA binding domain of the PSMAxCD3 bispecific single chain antibody of the invention are cross-species specific, i.e. reactive with the human and non-chimpanzee primates' antigens, it can be used both for preclinical evaluation of safety, activity and/or pharmacokinetic profile of these binding domains in primates and - in the identical form - as drug in humans. It will be understood that in a preferred embodiment, the cross-species specificity of the first and second binding domain of the antibodies of the invention is identical.

[0023] It has been found in the present invention that it is possible to generate a, preferably human, PSMAxCD3 bispecific single chain antibody wherein the identical molecule can be used in preclinical animal testing, as well as clinical studies and even in therapy in human. This is due to the unexpected identification of the, preferably human, PSMAxCD3 bispecific single chain antibody, which, in addition to binding to human CD3 epsilon and PSMA, respectively, (and due to genetic similarity likely to the chimpanzee counterpart), also binds to the homologs of said antigens of non-chimpanzee primates, including New-World Monkeys and Old-World Monkeys. As shown in the following Examples, said preferably human, PSMAxCD3 bispecific single chain antibody of the invention can be used as therapeutic agent against various diseases, including, but not limited, to cancer. The PSMAxCD3 bispecific single chain antibody is particularly advantageous for the therapy of cancer, preferably solid tumors, more preferably carcinomas and prostate cancer. In view of the above, the need to construct a surrogate PSMAxCD3 bispecific single chain antibody for testing in a phylogenetic distant (from humans) species disappears. As a result, the identical molecule can be used in animal preclinical testing as is intended to be administered to humans in clinical testing as well as following market approval and therapeutic drug administration. The ability to use the same molecule for preclinical animal testing as in later administration to humans virtually eliminates, or at least greatly reduces, the danger that the data obtained in preclinical animal testing have limited

applicability to the human case. In short, obtaining preclinical safety data in animals using the same molecule as will actually be administered to humans does much to ensure the applicability of the data to a human-relevant scenario. In contrast, in conventional approaches using surrogate molecules, said surrogate molecules have to be molecularly adapted to the animal test system used for preclinical safety assessment. Thus, the molecule to be used in human therapy in fact differs in sequence and also likely in structure from the surrogate molecule used in preclinical testing in pharmacokinetic parameters and/or biological activity, with the consequence that data obtained in preclinical animal testing have limited applicability / transferability to the human case. The use of surrogate molecules requires the construction, production, purification and characterization of a completely new construct. This leads to additional development costs and time necessary to obtain that molecule. In sum, surrogates have to be developed separately in addition to the actual drug to be used in human therapy, so that two lines of development for two molecules have to be carried out. Therefore, a major advantage of the, preferably human, PSMAxCD3 bispecific single chain antibody of the invention exhibiting cross-species specificity described herein is that the identical molecule can be used for therapeutic agents in humans and in preclinical animal testing.

[0024] It is preferred that at least one of said first or second binding domains of the bispecific single chain antibody of the invention is CDR-grafted, humanized or human, as set forth in more detail below. Preferably, both the first and second binding domains of the bispecific single chain antibody of the invention are CDR-grafted, humanized or human. For the preferably human, PSMAxCD3 bispecific single chain antibody of the invention, the generation of an immune reaction against said binding molecule is excluded to the maximum possible extent upon administration of the molecule to human patients.

[0025] Another major advantage of the, preferably human, PSMAxCD3 bispecific single chain antibody of the invention is its applicability for preclinical testing in various primates. The behavior of a drug candidate in animals should ideally be indicative of the expected behavior of this drug candidate upon administration to humans. As a result, the data obtained from such preclinical testing should therefore generally have a highly predictive power for the human case. However, as learned from the tragic outcome of the recent Phase I clinical trial on TGN1412 (a CD28 monoclonal antibody), a drug candidate may act differently in a primate species than in humans: Whereas in preclinical testing of said antibody no or only limited adverse effects have been observed in animal studies performed with cynomolgus monkeys, six human patients developed multiple organ failure upon administration of said antibody (Lancet 368 (2006), 2206-7). The results of these dramatic, non-desired negative events suggest that it may not be sufficient to limit preclinical testing to only one (non-chimpanzee primate) species. The fact that the PSMAxCD3 bispecific single chain antibody of the invention binds to a series of New-World and Old-World Monkeys may help to overcome the problems faced in the case mentioned above. Accordingly, the present invention provides means and methods for minimizing species differences in effects when drugs for human therapy are being developed and tested.

[0026] With the, preferably human, cross-species specific PSMAxCD3 bispecific single chain antibody of the invention it is also no longer necessary to adapt the test animal to the drug candidate intended for administration to humans, such as e.g. the creation of transgenic animals. The, preferably human, PSMAxCD3 bispecific single chain antibody of the invention exhibiting cross-species specificity according to the uses and the methods of invention can be directly used for preclinical testing in non-chimpanzee primates, without any genetic manipulation of the animals. As well known to those skilled in the art, approaches in which the test animal is adapted to the drug candidate always bear the risk that the results obtained in the preclinical safety testing are less representative and predictive for humans due to the modification of the animal. For example, in transgenic animals, the proteins encoded by the transgenes are often highly over-expressed. Thus, data obtained for the biological activity of an antibody against this protein antigen may be limited in their predictive value for humans in which the protein is expressed at much lower, more physiological levels.

[0027] A further advantage of the uses of the preferably human PSMAxCD3 bispecific single chain antibody of the invention exhibiting cross-species specificity is the fact that chimpanzees as an endangered species are avoided for animal testing. Chimpanzees are the closest relatives to humans and were recently grouped into the family of hominids based on the genome sequencing data (Wildman et al., PNAS 100 (2003), 7181). Therefore, data obtained with chimpanzee is generally considered to be highly predictive for humans. However, due to their status as endangered species, the number of chimpanzees, which can be used for medical experiments, is highly restricted. As stated above, maintenance of chimpanzees for animal testing is therefore both costly and ethically problematic. The uses of the, preferably human, PSMAxCD3 bispecific single chain antibody of the invention avoid both ethical objections and financial burden during preclinical testing without prejudicing the quality, i.e. applicability, of the animal testing data obtained. In light of this, the uses of the, preferably human, PSMAxCD3 bispecific single chain antibody of the invention provide for a reasonable alternative for studies in chimpanzees.

[0028] A still further advantage of the, preferably human, PSMAxCD3 bispecific single chain antibody of the invention is the ability of extracting multiple blood samples when using it as part of animal preclinical testing, for example in the course of pharmacokinetic animal studies. Multiple blood extractions can be much more readily obtained with a non-chimpanzee primate than with lower animals, e.g. a mouse. The extraction of multiple blood samples allows continuous testing of blood parameters for the determination of the biological effects induced by the, preferably human, PSMAxCD3

bispecific single chain antibody of the invention. Furthermore, the extraction of multiple blood samples enables the researcher to evaluate the pharmacokinetic profile of the, preferably human, PSMAxCD3 bispecific single chain antibody of the invention as defined herein. In addition, potential side effects, which may be induced by said, preferably human, PSMAxCD3 bispecific single chain antibody of the invention reflected in blood parameters can be measured in different

blood samples extracted during the course of the administration of said antibody.

[0029] This allows the determination of the potential toxicity profile of the, preferably human, PSMAxCD3 bispecific single chain antibody of the invention as defined herein.

[0030] The advantages of the, preferably human, PSMAxCD3 bispecific single chain antibody of the invention as defined herein exhibiting cross-species specificity may be briefly summarized as follows:

First, the, preferably human, PSMAxCD3 bispecific single chain antibody of the invention as defined herein used in preclinical testing is the same as the one used in human therapy. Thus, it is no longer necessary to develop two independent molecules, which may differ in their pharmacokinetic properties and biological activity. This is highly advantageous in that e.g. the pharmacokinetic results are more directly transferable and applicable to the human setting than e.g. in conventional surrogate approaches.

Second, the uses of the, preferably human, PSMAxCD3 bispecific single chain antibody of the invention as defined herein for the preparation of therapeutics in human is less cost- and labor-intensive than surrogate approaches.

Third, the, preferably human, PSMAxCD3 bispecific single chain antibody of the invention as defined herein can be used for preclinical testing not only in one primate species, but in a series of different primate species, thereby limiting the risk of potential species differences between primates and human.

Fourth, chimpanzee as an endangered species for animal testing can be avoided if desired.

Fifth, multiple blood samples can be extracted for extensive pharmacokinetic studies. Sixth, due to the human origin of the, preferably human, binding molecules according to a preferred embodiment of the invention, the generation of an immune reaction against said binding molecules is minimized when administered to human patients. Induction of an immune response with antibodies specific for a drug candidate derived from a non-human species as e.g. a mouse leading to the development of human-anti-mouse antibodies (HAMAs) against therapeutic molecules of murine origin is excluded.

Last but not least, the therapeutic use of the PSMAxCD3 bispecific single chain antibody of the invention provides a novel and inventive therapeutic approach for cancer, preferably solid tumors, more preferably carcinomas and prostate cancer. As shown in the following examples, the PSMAxCD3 bispecific single chain antibody of the invention provides an advantageous tool in order to kill PSMA-expressing human prostate cancer cells. Moreover, the cytotoxic activity of the PSMAxCD3 bispecific single chain antibody of the invention is higher than the activity of antibodies described in the art.

As noted herein above, the present invention provides polypeptides, i.e. bispecific single chain antibodies, comprising a first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 ϵ chain and a second binding domain capable of binding to PSMA. The second binding domain preferably binds to human PSMA and a non-chimpanzee primate PSMA. The advantage of bispecific single chain antibody molecules as drug candidates fulfilling the requirements of the preferred bispecific single chain antibody of the invention is the use of such molecules in preclinical animal testing as well as in clinical studies and even for therapy in human. In a preferred embodiment of the cross-species specific bispecific single chain antibodies of the invention the second binding domain binding to PSMA is human. In a cross-species specific bispecific molecule according to the invention the binding domain binding to an epitope of human and non-chimpanzee primate CD3 epsilon chain is located in the order VH-VL or VL-VH at the N-terminus or the C-terminus of the bispecific molecule. Examples for cross-species specific bispecific molecules according to the invention in different arrangements of the VH- and the VL-chain in the first and the second binding domain are described in the appended examples.

As used herein, a "bispecific single chain antibody" denotes a single polypeptide chain comprising two binding domains. Each binding domain comprises one variable region from an antibody heavy chain ("VH region"), wherein the VH region of the first binding domain specifically binds to the CD3 ϵ molecule, and the VH region of the second binding domain specifically binds to PSMA. The two binding domains are optionally linked to one another by a short polypeptide spacer. A non-limiting example for a polypeptide spacer is Gly-Gly-Gly-Gly-Ser (G-G-G-G-S) and repeats thereof. Each binding domain may additionally comprise one variable region from an antibody light chain ("VL region"), the VH region and VL region within each of the first and second binding domains being linked to one another via a polypeptide linker, for example of the type disclosed and claimed in EP 623679 B1, but in any case long enough to allow the VH region and VL region of the first binding domain and the VH region and VL region of the second binding domain to pair with one another such that, together, they are able to specifically bind to the respective first and second binding domains.

The term "protein" is well known in the art and describes biological compounds. Proteins comprise one or more amino acid chains (polypeptides), whereby the amino acids are bound among one another via a peptide bond. The term "polypeptide" as used herein describes a group of molecules, which consists of more than 30 amino acids. In accordance with the invention, the group of polypeptides comprises "proteins" as long as the proteins consist of a single polypeptide

chain. Also in line with the definition the term "polypeptide" describes fragments of proteins as long as these fragments consist of more than 30 amino acids. Polypeptides may further form multimers such as dimers, trimers and higher oligomers, i.e. consisting of more than one polypeptide molecule. Polypeptide molecules forming such dimers, trimers etc. may be identical or non-identical. The corresponding higher order structures of such multimers are, consequently, termed homo- or heterodimers, homo- or heterotrimers etc. An example for a heteromultimer is an antibody molecule, which, in its naturally occurring form, consists of two identical light polypeptide chains and two identical heavy polypeptide chains. The terms "polypeptide" and "protein" also refer to naturally modified polypeptides/proteins wherein the modification is effected e.g. by post-translational modifications like glycosylation, acetylation, phosphorylation and the like. Such modifications are well known in the art.

[0039] The term "binding domain" characterizes in connection with the present invention a domain of a polypeptide which specifically binds to/interacts with a given target structure/antigen/epitope. Thus, the binding domain is an "antigen-interaction-site". The term "antigen-interaction-site" defines, in accordance with the present invention, a motif of a polypeptide, which is able to specifically interact with a specific antigen or a specific group of antigens, e.g. the identical antigen in different species. Said binding/interaction is also understood to define a "specific recognition". The term "specifically recognizing" means in accordance with this invention that the antibody molecule is capable of specifically interacting with and/or binding to at least two, preferably at least three, more preferably at least four amino acids of an antigen, e.g. the human CD3 antigen as defined herein. Such binding may be exemplified by the specificity of a "lock-and-key-principle". Thus, specific motifs in the amino acid sequence of the binding domain and the antigen bind to each other as a result of their primary, secondary or tertiary structure as well as the result of secondary modifications of said structure. The specific interaction of the antigen-interaction-site with its specific antigen may result as well in a simple binding of said site to the antigen. Moreover, the specific interaction of the binding domain/antigen-interaction-site with its specific antigen may alternatively result in the initiation of a signal, e.g. due to the induction of a change of the conformation of the antigen, an oligomerization of the antigen, etc. A preferred example of a binding domain in line with the present invention is an antibody. The binding domain may be a monoclonal or polyclonal antibody or derived from a monoclonal or polyclonal antibody.

[0040] The term "antibody" comprises derivatives or functional fragments thereof which still retain the binding specificity. Techniques for the production of antibodies are well known in the art and described, e.g. in Harlow and Lane "Antibodies, A Laboratory Manual", Cold Spring Harbor Laboratory Press, 1988 and Harlow and Lane "Using Antibodies: A Laboratory Manual" Cold Spring Harbor Laboratory Press, 1999. The term "antibody" also comprises immunoglobulins (Ig's) of different classes (i.e. IgA, IgG, IgM, IgD and IgE) and subclasses (such as IgG1, IgG2 etc.).

[0041] The definition of the term "antibody" also includes embodiments such as chimeric, single chain and humanized antibodies, as well as antibody fragments, like, inter alia, Fab fragments. Antibody fragments or derivatives further comprise $F(ab')_2$, Fv, scFv fragments or single domain antibodies, single variable domain antibodies or immunoglobulin single variable domain comprising merely one variable domain, which might be VH or VL, that specifically bind to an antigen or epitope independently of other V regions or domains; see, for example, Harlow and Lane (1988) and (1999), loc. cit. Such immunoglobulin single variable domain encompasses not only an isolated antibody single variable domain polypeptide, but also larger polypeptides that comprise one or more monomers of an antibody single variable domain polypeptide sequence.

[0042] Various procedures are known in the art and may be used for the production of such antibodies and/or fragments. Thus, the (antibody) derivatives can also be produced by peptidomimetics. Further, techniques described for the production of single chain antibodies (see, inter alia, US Patent 4,946,778) can be adapted to produce single chain antibodies specific for elected polypeptide(s). Also, transgenic animals may be used to express humanized or human antibodies specific for polypeptides and fusion proteins of this invention. For the preparation of monoclonal antibodies, any technique, providing antibodies produced by continuous cell line cultures can be used. Examples for such techniques include the hybridoma technique (Köhler and Milstein Nature 256 (1975), 495-497), the trioma technique, the human B-cell hybridoma technique (Kozbor, Immunology Today 4 (1983), 72) and the EBV-hybridoma technique to produce human monoclonal antibodies (Cole et al., Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, Inc. (1985), 77-96). Surface plasmon resonance as employed in the BIAcore system can be used to increase the efficiency of phage antibodies which bind to an epitope of a target polypeptide, such as CD3 epsilon or PSMA (Schier, Human Antibodies Hybridomas 7 (1996), 97-105; Malmberg, J. Immunol. Methods 183 (1995), 7-13). It is also envisaged in the context of this invention that the term "antibody" comprises antibody constructs, which may be expressed in a host as described herein below, e.g. antibody constructs which may be transfected and/or transduced via, inter alia, viruses or plasmid vectors.

[0043] The term "specific interaction" as used in accordance with the present invention means that the binding domain does not or does not significantly cross-react with polypeptides which have similar structure as those bound by the binding domain, and which might be expressed by the same cells as the polypeptide of interest. Cross-reactivity of a panel of binding domains under investigation may be tested, for example, by assessing binding of said panel of binding domains under conventional conditions (see, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, 1988 and Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press,

1999). Examples for the specific interaction of a binding domain with a specific antigen comprise the specificity of a ligand for its receptor. Said definition particularly comprises the interaction of ligands, which induce a signal upon binding to its specific receptor. Examples for said interaction, which is also particularly comprised by said definition, is the interaction of an antigenic determinant (epitope) with the binding domain (antigenic binding site) of an antibody.

5 **[0044]** The term "cross-species specificity" or "interspecies specificity" as used herein means binding of a binding domain described herein to the same target molecule in humans and non-chimpanzee primates. Thus, "cross-species specificity" or "interspecies specificity" is to be understood as an interspecies reactivity to the same molecule "X" expressed in different species, but not to a molecule other than "X". Cross-species specificity of a monoclonal antibody recognizing e.g. human CD3 epsilon, to a non-chimpanzee primate CD3 epsilon, e.g. macaque CD3 epsilon, can be
10 determined, for instance, by FACS analysis. The FACS analysis is carried out in a way that the respective monoclonal antibody is tested for binding to human and non-chimpanzee primate cells, e.g. macaque cells, expressing said human and non-chimpanzee primate CD3 epsilon antigens, respectively. An appropriate assay is shown in the following examples. The above-mentioned subject matter applies mutatis mutandis for the PSMA antigen: Cross-species specificity of a monoclonal antibody recognizing e.g. human PSMA, to a non-chimpanzee primate PSMA, e.g. macaque PSMA, can
15 be determined, for instance, by FACS analysis. The FACS analysis is carried out in a way that the respective monoclonal antibody is tested for binding to human and non-chimpanzee primate cells, e.g. macaque cells, expressing said human and non-chimpanzee primate PSMA antigens, respectively.

[0045] As used herein, CD3 epsilon denotes a molecule expressed as part of the T cell receptor and has the meaning as typically ascribed to it in the prior art. In human, it encompasses in individual or independently combined form all
20 known CD3 subunits, for example CD3 epsilon, CD3 delta, CD3 gamma, CD3 zeta, CD3 alpha and CD3 beta. The non-chimpanzee primate, non-human CD3 antigens as referred to herein are, for example, *Macaca fascicularis* CD3 and *Macaca mulatta* CD3. In *Macaca fascicularis*, it encompasses CD3 epsilon FN-18 negative and CD3 epsilon FN-18 positive, CD3 gamma and CD3 delta. In *Macaca mulatta*, it encompasses CD3 epsilon, CD3 gamma and CD3 delta. Preferably, said CD3 as used herein is CD3 epsilon.

25 **[0046]** The human CD3 epsilon is indicated in GenBank Accession No. NM_000733 and comprises SEQ ID NO. 1. The human CD3 gamma is indicated in GenBank Accession NO. NM_000073. The human CD3 delta is indicated in GenBank Accession No. NM_000732.

[0047] The CD3 epsilon "FN-18 negative" of *Macaca fascicularis* (i.e. CD3 epsilon not recognized by monoclonal antibody FN-18 due to a polymorphism as set forth above) is indicated in GenBank Accession No. AB073994.

30 **[0048]** The CD3 epsilon "FN-18 positive" of *Macaca fascicularis* (i.e. CD3 epsilon recognized by monoclonal antibody FN-18) is indicated in GenBank Accession No. AB073993. The CD3 gamma of *Macaca fascicularis* is indicated in GenBank Accession No. AB073992. The CD3 delta of *Macaca fascicularis* is indicated in GenBank Accession No. AB073991.

35 **[0049]** The nucleic acid sequences and amino acid sequences of the respective CD3 epsilon, gamma and delta homologs of *Macaca mulatta* can be identified and isolated by recombinant techniques described in the art (Sambrook et al. Molecular Cloning: A Laboratory Manual; Cold Spring Harbor Laboratory Press, 3rd edition 2001). This applies mutatis mutandis to the CD3 epsilon, gamma and delta homologs of other non-chimpanzee primates as defined herein. The identification of the amino acid sequence of *Callithrix jacchus*, *Saimiri sciureus* und *Saguinus oedipus* is described in the appended examples. The amino acid sequence of the extracellular domain of the CD3 epsilon of *Callithrix jacchus*
40 is depicted in SEQ ID NO: 3, the one of *Saguinus oedipus* is depicted in SEQ ID NO: 5 and the one of *Saimiri sciureus* is depicted in SEQ ID NO: 7.

[0050] The human PSMA is indicated in GenBank Accession No. 'AY101595'. The cloning of the PSMA homolog of macaque is demonstrated in the following examples, the corresponding cDNA and amino acid sequences are shown in SEQ ID NOs. 385 and 386, respectively.

45 **[0051]** In line with the above, the term "epitope" defines an antigenic determinant, which is specifically bound/identified by a binding domain as defined herein. The binding domain may specifically bind to/interact with conformational or continuous epitopes, which are unique for the target structure, e.g. the human and non-chimpanzee primate CD3 epsilon chain or the human and non-chimpanzee primate PSMA. A conformational or discontinuous epitope is characterized for polypeptide antigens by the presence of two or more discrete amino acid residues which are separated in the primary
50 sequence, but come together on the surface of the molecule when the polypeptide folds into the native protein/antigen (Sela, (1969) Science 166, 1365 and Laver, (1990) Cell 61, 553-6). The two or more discrete amino acid residues contributing to the epitope are present on separate sections of one or more polypeptide chain(s). These residues come together on the surface of the molecule when the polypeptide chain(s) fold(s) into a three-dimensional structure to constitute the epitope. In contrast, a continuous or linear epitope consists of two or more discrete amino acid residues,
55 which are present in a single linear segment of a polypeptide chain. Within the present invention, a "context-dependent" CD3 epitope refers to the conformation of said epitope. Such a context-dependent epitope, localized on the epsilon chain of CD3, can only develop its correct conformation if it is embedded within the rest of the epsilon chain and held in the right position by heterodimerization of the epsilon chain with either CD3 gamma or delta chain. In contrast, a

context-independent CD3 epitope as provided herein refers to an N-terminal 1-27 amino acid residue polypeptide or a functional fragment thereof of CD3 epsilon. This N-terminal 1-27 amino acid residue polypeptide or a functional fragment thereof maintains its three-dimensional structural integrity and correct conformation when taken out of its native environment in the CD3 complex. The context-independency of the N-terminal 1-27 amino acid residue polypeptide or a functional fragment thereof, which is part of the extracellular domain of CD3 epsilon, represents, thus, an epitope which is completely different to the epitopes of CD3 epsilon described in connection with a method for the preparation of human binding molecules in WO 2004/106380. Said method used solely expressed recombinant CD3 epsilon. The conformation of this solely expressed recombinant CD3 epsilon differed from that adopted in its natural form, that is, the form in which the CD3 epsilon subunit of the TCR/CD3 complex exists as part of a noncovalent complex with either the CD3 delta or the CD3-gamma subunit of the TCR/CD3 complex. When such solely expressed recombinant CD3 epsilon protein is used as an antigen for selection of antibodies from an antibody library, antibodies specific for this antigen are identified from the library although such a library does not contain antibodies with specificity for self-antigens/autoantigens. This is due to the fact that solely expressed recombinant CD3 epsilon protein does not exist *in vivo*; it is not an autoantigen. Consequently, subpopulations of B cells expressing antibodies specific for this protein have not been depleted *in vivo*; an antibody library constructed from such B cells would contain genetic material for antibodies specific for solely expressed recombinant CD3 epsilon protein.

[0052] However, since the context-independent N-terminal 1-27 amino acid residue polypeptide or a functional fragment thereof is an epitope, which folds in its native form, binding domains in line with the present invention cannot be identified by methods based on the approach described in WO 2004/106380. Therefore, it could be verified in tests that binding molecules as disclosed in WO 2004/106380 are not capable of binding to the N-terminal 1-27 amino acid residues of the CD3 epsilon chain. Hence, conventional anti-CD3 binding molecules or anti-CD3 antibody molecules (e.g. as disclosed in WO 99/54440) bind CD3 epsilon chain at a position which is more C-terminally located than the context-independent N-terminal 1-27 amino acid residue polypeptide or a functional fragment provided herein. Prior art antibody molecules OKT3 and UCHT-1 have also a specificity for the epsilon-subunit of the TCR/CD3 complex between amino acid residues 35 to 85 and, accordingly, the epitope of these antibodies is also more C-terminally located. In addition, UCHT-1 binds to the CD3 epsilon chain in a region between amino acid residues 43 to 77 (Tunncliffe, *Int. Immunol.* 1 (1989), 546-50; Kjer-Nielsen, *PNAS* 101, (2004), 7675-7680; Salmeron, *J. Immunol.* 147 (1991), 3047-52). Therefore, prior art anti-CD3 molecules do not bind to and are not directed against the herein defined context-independent N-terminal 1-27 amino acid residue epitope (or a functional fragment thereof). In particular, the state of the art fails to provide anti-CD3 molecules which specifically binds to the context-independent N-terminal 1-27 amino acid residue epitope and which are cross-species specific, i.e. bind to human and non-chimpanzee primate CD3 epsilon.

[0053] For the generation of a, preferably human, binding domain comprised in a bispecific single chain antibody molecule of the invention, e.g. monoclonal antibodies binding to both the human and non-chimpanzee primate CD3 epsilon (e.g. macaque CD3 epsilon) or monoclonal antibodies binding to both the human and non-chimpanzee primate PSMA can be used.

[0054] As used herein, "human" and "man" refers to the species *Homo sapiens*. As far as the medical uses of the constructs described herein are concerned, human patients are to be treated with the same molecule.

[0055] It is preferred that at least one of said first or second binding domains of the bispecific single chain antibody of the invention is CDR-grafted, humanized or human. Preferably, both the first and second binding domains of the bispecific single chain antibody of the invention are CDR-grafted, humanized or human.

[0056] The term "human" antibody as used herein is to be understood as meaning that the bispecific single chain antibody as defined herein, comprises (an) amino acid sequence(s) contained in the human germline antibody repertoire. For the purposes of definition herein, said bispecific single chain antibody may therefore be considered human if it consists of such (a) human germline amino acid sequence(s), i.e. if the amino acid sequence(s) of the bispecific single chain antibody in question is (are) identical to (an) expressed human germline amino acid sequence(s). A bispecific single chain antibody as defined herein may also be regarded as human if it consists of (a) sequence(s) that deviate(s) from its (their) closest human germline sequence(s) by no more than would be expected due to the imprint of somatic hypermutation. Additionally, the antibodies of many non-human mammals, for example rodents such as mice and rats, comprise VH CDR3 amino acid sequences which one may expect to exist in the expressed human antibody repertoire as well. Any such sequence(s) of human or non-human origin which may be expected to exist in the expressed human repertoire would also be considered "human" for the purposes of the present invention.

[0057] As used herein, the term "humanized", "humanization", "human-like" or grammatically related variants thereof are used interchangeably to refer to a bispecific single chain antibody comprising in at least one of its binding domains at least one complementarity determining region ("CDR") from a non-human antibody or fragment thereof. Humanization approaches are described for example in WO 91/09968 and US 6,407,213. As non-limiting examples, the term encompasses the case in which a variable region of at least one binding domain comprises a single CDR region, for example the third CDR region of the VH (CDRH3), from another non-human animal, for example a rodent, as well as the case in which a or both variable region/s comprise at each of their respective first, second and third CDRs the CDRs from said

non-human animal. In the event that all CDRs of a binding domain of the bispecific single chain antibody have been replaced by their corresponding equivalents from, for example, a rodent, one typically speaks of "CDR-grafting", and this term is to be understood as being encompassed by the term "humanized" or grammatically related variants thereof as used herein. The term "humanized" or grammatically related variants thereof also encompasses cases in which, in addition to replacement of one or more CDR regions within a VH and/or VL of the first and/or second binding domain further mutation/s (e.g. substitutions) of at least one single amino acid residue/s within the framework ("FR") regions between the CDRs has/have been effected such that the amino acids at that/those positions correspond/s to the amino acid/s at that/those position/s in the animal from which the CDR regions used for replacement is/are derived. As is known in the art, such individual mutations are often made in the framework regions following CDR-grafting in order to restore the original binding affinity of the non-human antibody used as a CDR-donor for its target molecule. The term "humanized" may further encompass (an) amino acid substitution(s) in the CDR regions from a non-human animal to the amino acid(s) of a corresponding CDR region from a human antibody, in addition to the amino acid substitutions in the framework regions as described above.

[0058] As used herein, the term "homolog" or "homology" is to be understood as follows: Homology among proteins and DNA is often concluded on the basis of sequence similarity, especially in bioinformatics. For example, in general, if two or more genes have highly similar DNA sequences, it is likely that they are homologous. But sequence similarity may arise from different ancestors: short sequences may be similar by chance, and sequences may be similar because both were selected to bind to a particular protein, such as a transcription factor. Such sequences are similar but not homologous. Sequence regions that are homologous are also called conserved. This is not to be confused with conservation in amino acid sequences in which the amino acid at a specific position has changed but the physio-chemical properties of the amino acid remain unchanged. Homologous sequences are of two types: orthologous and paralogous. Homologous sequences are orthologous if they were separated by a speciation event: when a species diverges into two separate species, the divergent copies of a single gene in the resulting species are said to be orthologous. Orthologs, or orthologous genes, are genes in different species that are similar to each other because they originated from a common ancestor. The strongest evidence that two similar genes are orthologous is the result of a phylogenetic analysis of the gene lineage. Genes that are found within one clade are orthologs, descended from a common ancestor. Orthologs often, but not always, have the same function. Orthologous sequences provide useful information in taxonomic classification studies of organisms. The pattern of genetic divergence can be used to trace the relatedness of organisms. Two organisms that are very closely related are likely to display very similar DNA sequences between two orthologs. Conversely, an organism that is further removed evolutionarily from another organism is likely to display a greater divergence in the sequence of the orthologs being studied. Homologous sequences are paralogous if they were separated by a gene duplication event: if a gene in an organism is duplicated to occupy two different positions in the same genome, then the two copies are paralogous. A set of sequences that are paralogous are called paralogs of each other. Paralogs typically have the same or similar function, but sometimes do not: due to lack of the original selective pressure upon one copy of the duplicated gene, this copy is free to mutate and acquire new functions. An example can be found in rodents such as rats and mice. Rodents have a pair of paralogous insulin genes, although it is unclear if any divergence in function has occurred. Paralogous genes often belong to the same species, but this is not necessary: for example, the hemoglobin gene of humans and the myoglobin gene of chimpanzees are paralogs. This is a common problem in bioinformatics: when genomes of different species have been sequenced and homologous genes have been found, one can not immediately conclude that these genes have the same or similar function, as they could be paralogs whose function has diverged.

[0059] As used herein, a "non-chimpanzee primate" or "non-chimp primate" or grammatical variants thereof refers to any primate animal (i.e. not human) other than chimpanzee, i.e. other than an animal of belonging to the genus *Pan*, and including the species *Pan paniscus* and *Pan troglodytes*, also known as *Anthropopithecus troglodytes* or *Simia satyrus*. It will be understood, however, that it is possible that the antibodies of the invention can also bind with their first and/or second binding domain to the respective epitopes/fragments etc. of said chimpanzees. The intention is merely to avoid animal tests which are carried out with chimpanzees, if desired. It is thus also envisaged that in another embodiment the antibodies of the present invention also bind with their first and/or second binding domain to the respective epitopes of chimpanzees. A "primate", "primate species", "primates" or grammatical variants thereof denote/s an order of eutherian mammals divided into the two suborders of prosimians and anthropoids and comprising apes, monkeys and lemurs. Specifically, "primates" as used herein comprises the suborder *Strepsirrhini* (non-tarsier prosimians), including the infraorder *Lemuriformes* (itself including the superfamilies *Cheirogaleoidea* and *Lemuroidea*), the infraorder *Chiromyiformes* (itself including the family *Daubentonidae*) and the infraorder *Lorisiformes* (itself including the families *Lorisiidae* and *Galagidae*). "Primates" as used herein also comprises the suborder *Haplorrhini*, including the infraorder *Tarsiiformes* (itself including the family *Tarsiidae*), the infraorder *Simiiformes* (itself including the *Platyrrhini*, or New-World monkeys, and the *Catarrhini*, including the *Cercopithecoidea*, or Old-World Monkeys).

[0060] The non-chimpanzee primate species may be understood within the meaning of the invention to be a lemur, a tarsier, a gibbon, a marmoset (belonging to New-World Monkeys of the family *Cebidae*) or an Old-World Monkey (be-

longing to the superfamily *Cercopithecoidea*).

[0061] As used herein, an "Old-World Monkey" comprises any monkey falling in the superfamily *Cercopithecoidea*, itself subdivided into the families: the *Cercopithecinae*, which are mainly African but include the diverse genus of macaques which are Asian and North African; and the *Colobinae*, which include most of the Asian genera but also the

5 African colobus monkeys.

[0062] Specifically, within the subfamily *Cercopithecinae*, an advantageous non-chimpanzee primate may be from the Tribe *Cercopithecini*, within the genus *Allenopithecus* (Allen's Swamp Monkey, *Allenopithecus nigroviridis*); within the genus *Miopithecus* (Angolan Talapoin, *Miopithecus talapoin*; Gabon Talapoin, *Miopithecus ogouensis*); within the genus *Erythrocebus* (Patas Monkey, *Erythrocebus patas*); within the genus *Chlorocebus* (Green Monkey, *Chlorocebus sa-*
10 *baceus*; Grivet, *Chlorocebus aethiops*; Bale Mountains Vervet, *Chlorocebus djamdjamensis*; Tantalus Monkey, *Chlorocebus tantalus*; Vervet Monkey, *Chlorocebus pygerythrus*; Malbrouck, *Chlorocebus cynosuros*); or within the genus *Cercopithecus* (Dryas Monkey or Salongo Monkey, *Cercopithecus dryas*; Diana Monkey, *Cercopithecus diana*; Roloway Monkey, *Cercopithecus roloway*; Greater Spot-nosed Monkey, *Cercopithecus nictitans*; Blue Monkey, *Cercopithecus mitis*; Silver Monkey, *Cercopithecus doggetti*; Golden Monkey, *Cercopithecus kandti*; Sykes's Monkey, *Cercopithecus albogularis*; Mona Monkey, *Cercopithecus mona*; Campbell's Mona Monkey, *Cercopithecus campbelli*; Lowe's Mona
15 Monkey, *Cercopithecus lowei*; Crested Mona Monkey, *Cercopithecus pogonias*; Wolfs Mona Monkey, *Cercopithecus wolffi*; Dent's Mona Monkey, *Cercopithecus denti*; Lesser Spot-nosed Monkey, *Cercopithecus petaurista*; White-throated Guenon, *Cercopithecus erythrogaster*; Sclater's Guenon, *Cercopithecus sclateri*; Red-eared Guenon, *Cercopithecus erythrotis*; Moustached Guenon, *Cercopithecus cephus*; Red-tailed Monkey, *Cercopithecus ascanius*; L'Hoest's Monkey, *Cercopithecus lhoesti*; Preuss's Monkey, *Cercopithecus preussi*; Sun-tailed Monkey, *Cercopithecus solatus*; Hamlyn's
20 Monkey or Owl-faced Monkey, *Cercopithecus hamlyni*; De Brazza's Monkey, *Cercopithecus neglectus*). Alternatively, an advantageous non-chimpanzee primate, also within the subfamily *Cercopithecinae* but within the Tribe *Papionini*, may be from within the genus *Macaca* (Barbary Macaque, *Macaca sylvanus*; Lion-tailed Macaque, *Macaca silenus*; Southern Pig-tailed Macaque or Beruk, *Macaca nemestrina*; Northern Pig-tailed Macaque, *Macaca leonina*; Pagai Island
25 Macaque or Bokkoi, *Macaca pagensis*; Siberut Macaque, *Macaca siberu*; Moor Macaque, *Macaca maura*; Booted Macaque, *Macaca ochreata*; Tonkean Macaque, *Macaca tonkeana*; Heck's Macaque, *Macaca hecki*; Gorontalo Macaque, *Macaca nigrescens*; Celebes Crested Macaque or Black "Ape", *Macaca nigra*; Cynomolgus monkey or Crab-eating Macaque or Long-tailed Macaque or Kera, *Macaca fascicularis*; Stump-tailed Macaque or Bear Macaque, *Macaca arctoides*; Rhesus Macaque, *Macaca mulatta*; Formosan Rock Macaque, *Macaca cyclopis*; Japanese Macaque, *Macaca fuscata*; Toque Macaque, *Macaca sinica*; Bonnet Macaque, *Macaca radiata*; Barbary Macaque, *Macaca sylvanus*; Assam Macaque, *Macaca assamensis*; Tibetan Macaque or Milne-Edwards' Macaque, *Macaca thibetana*; Arunachal
30 Macaque or Munzala, *Macaca munzala*); within the genus *Lophocebus* (Gray-cheeked Mangabey, *Lophocebus albigena*; *Lophocebus albigena albigena*; *Lophocebus albigena osmani*; *Lophocebus albigena johnstoni*; Black Crested Mangabey, *Lophocebus aterrimus*; Opdenbosch's Mangabey, *Lophocebus opdenboschi*; Highland Mangabey, *Lophocebus kipunji*); within the genus *Papio* (Hamadryas Baboon, *Papio hamadryas*; Guinea Baboon, *Papio papio*; Olive Baboon, *Papio anubis*; Yellow Baboon, *Papio cynocephalus*; Chacma Baboon, *Papio ursinus*); within the genus *Theropithecus* (Gelada, *Theropithecus gelada*); within the genus *Cercocebus* (Sooty Mangabey, *Cercocebus atys*; *Cercocebus atys atys*; *Cercocebus atys lunulatus*; Collared Mangabey, *Cercocebus torquatus*; Agile Mangabey, *Cercocebus agilis*; Golden-bellied Mangabey, *Cercocebus chrysogaster*; Tana River Mangabey, *Cercocebus galeritus*; Sanje Mangabey, *Cercocebus sanjei*); or within the genus *Mandrillus* (Mandrill, *Mandrillus sphinx*; Drill, *Mandrillus leucophaeus*).

[0063] Most preferred is *Macaca fascicularis* (also known as Cynomolgus monkey and, therefore, in the Examples named "Cynomolgus") and *Macaca mulatta* (rhesus monkey, named "rhesus").

[0064] Within the subfamily *Colobinae*, an advantageous non-chimpanzee primate may be from the African group, within the genus *Colobus* (Black Colobus, *Colobus satanas*; Angola Colobus, *Colobus angolensis*; King Colobus, *Colobus polykomos*; Ursine Colobus, *Colobus vellerosus*; Mantled Guereza, *Colobus guereza*); within the genus *Piliocolobus* (Western Red Colobus, *Piliocolobus badius*; *Piliocolobus badius badius*; *Piliocolobus badius temminckii*; *Piliocolobus badius viraldronae*; Pennant's Colobus, *Piliocolobus pennantii*; *Piliocolobus pennantii pennantii*; *Piliocolobus pennantii epieni*; *Piliocolobus pennantii bouvieri*; Preuss's Red Colobus, *Piliocolobus preussi*; Thollon's Red Colobus, *Piliocolobus tholloni*; Central African Red Colobus, *Piliocolobus foai*; *Piliocolobus foai foai*; *Piliocolobus foai ellioti*; *Piliocolobus foai oustalefi*; *Piliocolobus foai semlikiensis*; *Piliocolobus foai parmentierorum*; Ugandan Red Colobus, *Piliocolobus fephrasceles*; Uzungwa Red Colobus, *Piliocolobus gordonorum*; Zanzibar Red Colobus, *Piliocolobus kirkii*; Tana River Red Colobus, *Piliocolobus rufomitrat*); or within the genus *Procolobus* (Olive Colobus, *Procolobus verus*).

[0065] Within the subfamily *Colobinae*, an advantageous non-chimpanzee primate may alternatively be from the Langur (leaf monkey) group, within the genus *Semnopithecus* (Nepal Gray Langur, *Semnopithecus schistaceus*; Kashmir Gray Langur, *Semnopithecus ajax*; Tarai Gray Langur, *Semnopithecus hector*; Northern Plains Gray Langur, *Semnopithecus entellus*; Black-footed Gray Langur, *Semnopithecus hypoleucos*; Southern Plains Gray Langur, *Semnopithecus dussumieri*; Tufted Gray Langur, *Semnopithecus priam*); within the *T. vetulus* group or the genus *Trachypithecus* (Purple-faced Langur, *Trachypithecus vetulus*; Nilgiri Langur, *Trachypithecus johnii*); within the *T. cristatus* group of the genus

Trachypithecus (Javan Lutung, *Trachypithecus auratus*; Silvery Leaf Monkey or Silvery Lutung, *Trachypithecus cristatus*; Indochinese Lutung, *Trachypithecus germaini*; Tenasserim Lutung, *Trachypithecus barbei*); within the *T. obscurus* group of the genus *Trachypithecus* (Dusky Leaf Monkey or Spectacled Leaf Monkey, *Trachypithecus obscurus*; Phayre's Leaf Monkey, *Trachypithecus phayrei*); within the *T. pileatus* group of the genus *Trachypithecus* (Capped Langur, *Trachypithecus pileatus*; Shortridge's Langur, *Trachypithecus shortridgei*; Gee's Golden Langur, *Trachypithecus geei*); within the *T. francoisi* group of the genus *Trachypithecus* (Francois' Langur, *Trachypithecus francoisi*; Hatinh Langur, *Trachypithecus hatinhensis*; White-headed Langur, *Trachypithecus poliocephalus*; Laotian Langur, *Trachypithecus laotum*; Delacour's Langur, *Trachypithecus delacouri*; Indochinese Black Langur, *Trachypithecus ebenus*); or within the genus *Presbytis* (Sumatran Surili, *Presbytis melalophos*; Banded Surili, *Presbytis femoralis*; Sarawak Surili, *Presbytis chrysomelas*; White-thighed Surili, *Presbytis siamensis*; White-fronted Surili, *Presbytis frontata*; Javan Surili, *Presbytis comata*; Thomas's Langur, *Presbytis thomasi*; Hose's Langur, *Presbytis hosei*; Maroon Leaf Monkey, *Presbytis rubicunda*; Mentawai Langur or Joja, *Presbytis potenziani*; Natuna Island Surili, *Presbytis natunae*).

[0066] Within the subfamily Colobinae, an advantageous non-chimpanzee primate may alternatively be from the Odd-Nosed group, within the genus *Pygathrix* (Red-shanked Douc, *Pygathrix nemaeus*; Black-shanked Douc, *Pygathrix nigripes*; Gray-shanked Douc, *Pygathrix cinerea*); within the genus *Rhinopithecus* (Golden Snub-nosed Monkey, *Rhinopithecus roxellana*; Black Snub-nosed Monkey, *Rhinopithecus bieti*; Gray Snub-nosed Monkey, *Rhinopithecus brelichi*; Tonkin Snub-nosed Langur, *Rhinopithecus avunculus*); within the genus *Nasalis* (Proboscis Monkey, *Nasalis larvatus*); or within the genus *Simias* (Pig-tailed Langur, *Simias concolor*).

[0067] As used herein, the term "marmoset" denotes any New-World Monkeys of the genus *Callithrix*, for example belonging to the Atlantic marmosets of subgenus *Callithrix* (sic!) (Common Marmoset, *Callithrix (Callithrix) jacchus*; Black-tufted Marmoset, *Callithrix (Callithrix) penicillata*; Wied's Marmoset, *Callithrix (Callithrix) kuhlii*; White-headed Marmoset, *Callithrix (Callithrix) geoffroyi*; Buffy-headed Marmoset, *Callithrix (Callithrix) flaviceps*; Buffy-tufted Marmoset, *Callithrix (Callithrix) aurita*); belonging to the Amazonian marmosets of subgenus *Mico* (Rio Acari Marmoset, *Callithrix (Mico) acariensis*; Manicore Marmoset, *Callithrix (Mico) manicorensis*; Silvery Marmoset, *Callithrix (Mico) argentata*; White Marmoset, *Callithrix (Mico) leucippe*; Emilia's Marmoset, *Callithrix (Mico) emiliae*; Black-headed Marmoset, *Callithrix (Mico) nigriceps*; Marca's Marmoset, *Callithrix (Mico) marcai*; Black-tailed Marmoset, *Callithrix (Mico) melanura*; Santarem Marmoset, *Callithrix (Mico) humeralifera*; Maués Marmoset, *Callithrix (Mico) mauesi*; Gold-and-white Marmoset, *Callithrix (Mico) chrysoleuca*; Hershkovitz's Marmoset, *Callithrix (Mico) intermedia*; Satéré Marmoset, *Callithrix (Mico) sateri*); Roosmalens' Dwarf Marmoset belonging to the subgenus *Callibella* (*Callithrix (Callibella) humilis*); or the Pygmy Marmoset belonging to the subgenus *Cebuella* (*Callithrix (Cebuella) pygmaea*).

[0068] Other genera of the New-World Monkeys comprise tamarins of the genus *Saguinus* (comprising the *S. oedipus*-group, the *S. midas* group, the *S. nigricollis* group, the *S. mystax* group, the *S. bicolor* group and the *S. inustus* group) and squirrel monkeys of the genus *Saimiri* (e.g. *Saimiri sciureus*, *Saimiri oerstedii*, *Saimiri ustus*, *Saimiri boliviensis*, *Saimiri vanzolini*).

[0069] In a preferred embodiment of the bispecific single chain antibody molecule of the invention, the non-chimpanzee primate is an old world monkey. In a more preferred embodiment of the polypeptide, the old world monkey is a monkey of the Papio genus Macaque genus. Most preferably, the monkey of the Macaque genus is Assamese macaque (*Macaca assamensis*), Barbary macaque (*Macaca sylvanus*), Bonnet macaque (*Macaca radiata*), Booted or Sulawesi-Booted macaque (*Macaca ochreata*), Sulawesi-crested macaque (*Macaca nigra*), Formosan rock macaque (*Macaca cyclopsis*), Japanese snow macaque or Japanese macaque (*Macaca fuscata*), Cynomolgus monkey or crab-eating macaque or long-tailed macaque or Java macaque (*Macaca fascicularis*), Lion-tailed macaque (*Macaca silenus*), Pigtailed macaque (*Macaca nemestrina*), Rhesus macaque (*Macaca mulatta*), Tibetan macaque (*Macaca thibetana*), Tonkean macaque (*Macaca tonkeana*), Toque macaque (*Macaca sinica*), Stump-tailed macaque or Red-faced macaque or Bear monkey (*Macaca arctoides*), or Moor macaque (*Macaca maurus*). Most preferably, the monkey of the Papio genus is *Hamadryas* Baboon, *Papio hamadryas*; Guinea Baboon, *Papio papio*; Olive Baboon, *Papio anubis*; Yellow Baboon, *Papio cynocephalus*; Chacma Baboon, *Papio ursinus*.

[0070] In an alternatively preferred embodiment of the bispecific single chain antibody molecule of the invention, the non-chimpanzee primate is a new world monkey. In a more preferred embodiment of the polypeptide, the new world monkey is a monkey of the *Callithrix* genus (marmoset), the *Saguinus* genus or the *Saimiri* genus. Most preferably, the monkey of the *Callithrix* genus is *Callithrix jacchus*, the monkey of the *Saguinus* genus is *Saguinus oedipus* and the monkey of the *Saimiri* genus is *Saimiri sciureus*.

[0071] The term "cell surface antigen" as used herein denotes a molecule, which is displayed on the surface of a cell. In most cases, this molecule will be located in or on the plasma membrane of the cell such that at least part of this molecule remains accessible from outside the cell in tertiary form. A non-limiting example of a cell surface molecule, which is located in the plasma membrane is a transmembrane protein comprising, in its tertiary conformation, regions of hydrophilicity and hydrophobicity. Here, at least one hydrophobic region allows the cell surface molecule to be embedded, or inserted in the hydrophobic plasma membrane of the cell while the hydrophilic regions extend on either side of the plasma membrane into the cytoplasm and extracellular space, respectively. Non-limiting examples of cell surface

molecules which are located on the plasma membrane are proteins which have been modified at a cysteine residue to bear a palmitoyl group, proteins modified at a C-terminal cysteine residue to bear a farnesyl group or proteins which have been modified at the C-terminus to bear a glycosyl phosphatidyl inositol ("GPI") anchor. These groups allow covalent attachment of proteins to the outer surface of the plasma membrane, where they remain accessible for recognition by extracellular molecules such as antibodies. Examples of cell surface antigens are CD3 epsilon and PSMA. As described herein above, PSMA is a cell surface antigen which is a target for therapy of cancer, including, but not limited to solid tumors, preferably carcinomas and prostate cancer.

[0072] In light of this, PSMA can also be characterized as a tumor antigen. The term "tumor antigen" as used herein may be understood as those antigens that are presented on tumor cells. These antigens can be presented on the cell surface with an extracellular part, which is often combined with a transmembrane and cytoplasmic part of the molecule. These antigens can sometimes be presented only by tumor cells and never by the normal ones. Tumor antigens can be exclusively expressed on tumor cells or might represent a tumor specific mutation compared to normal cells. In this case, they are called tumor-specific antigens. More common are antigens that are presented by tumor cells and normal cells, and they are called tumor-associated antigens. These tumor-associated antigens can be overexpressed compared to normal cells or are accessible for antibody binding in tumor cells due to the less compact structure of the tumor tissue compared to normal tissue. One example for a tumor antigen in line with the present invention is PSMA.

[0073] As described herein above the bispecific single chain antibody molecule of the invention binds with the first binding domain to an epitope of human and non-chimpanzee primate CD3 ϵ (epsilon) chain, wherein the epitope is part of an amino acid sequence comprised in the group consisting of 27 amino acid residues as depicted in SEQ ID NOs. 2, 4, 6, or 8 or a functional fragment thereof.

[0074] In line with the present invention it is preferred for the bispecific single chain antibody molecule of the invention that said epitope is part of an amino acid sequence comprising 26, 25, 24, 23, 22, 21, 20, 19, 18, 17, 16, 15, 14, 13, 12, 11, 10, 9, 8, 7, 6 or 5 amino acids.

[0075] More preferably, wherein said epitope comprises at least the amino acid sequence Gln-Asp-Gly-Asn-Glu (Q-D-G-N-E).

[0076] Within the present invention, a functional fragment of the N-terminal 1-27 amino acid residues means that said functional fragment is still a context-independent epitope maintaining its three-dimensional structural integrity when taken out of its native environment in the CD3 complex (and fused to a heterologous amino acid sequence such as EpCAM or an immunoglobulin Fc part, e.g. as shown in Example 3.1). The maintenance of the three-dimensional structure within the 27 amino acid N-terminal polypeptide or functional fragment thereof of CD3 epsilon can be used for the generation of binding domains which bind to the N-terminal CD3 epsilon polypeptide fragment *in vitro* and to the native (CD3 epsilon subunit of the) CD3 complex on T cells *in vivo* with the same binding affinity. Within the present invention, a functional fragment of the N-terminal 1-27 amino acid residues means that CD3 binding domains provided herein can still bind to such functional fragments in a context-independent manner. The person skilled in the art is aware of methods for epitope mapping to determine which amino acid residues of an epitope are recognized by such anti-CD3 binding domains (e.g. alanine scanning; see appended examples).

[0077] In one embodiment of the invention, the bispecific single chain antibody molecule of the invention comprises a (first) binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 ϵ chain and a second binding domain capable of binding to the cell surface antigen PSMA.

[0078] Within the present invention it is further preferred that the second binding domain binds to the human cell surface antigen PSMA and/or a non-chimpanzee primate PSMA. Particularly preferred, the second binding domain binds to the human PSMA and a non-chimpanzee primate PSMA, preferably a macaque PSMA. It is to be understood, that the second binding domain binds to at least one non-chimpanzee primate PSMA, however, it may also bind to two, three or more, non-chimpanzee primate PSMA homologs. For example, the second binding domain may bind to the Cynomolgus monkey PSMA and to the Rhesus monkey PSMA.

[0079] The present invention including all methods, uses, kits etc. described herein, also relates to the second binding domains as such (i.e. not in the context of a bispecific single chain antibody). "As such" further includes antibody formats other than the bispecific single chain antibodies as described herein, for example antibody fragments (comprising the second domain), humanized antibodies, fusion proteins comprising the second domain etc. Antibody formats other than the bispecific single chain antibodies of the present invention are also described herein above.

[0080] For the generation of the second binding domain of the bispecific single chain antibody molecule of the invention, e.g. bispecific single chain antibodies as defined herein, monoclonal antibodies binding to both of the respective human and/or non-chimpanzee primate cell surface antigen such as PSMA can be utilized. Appropriate binding domains for the bispecific polypeptide as defined herein e.g. can be derived from cross-species specific monoclonal antibodies by recombinant methods described in the art. A monoclonal antibody binding to a human cell surface antigen and to the homolog of said cell surface antigen in a non-chimpanzee primate can be tested by FACS assays as set forth above. It is evident to those skilled in the art that cross-species specific antibodies can also be generated by hybridoma techniques described in the literature (Milstein and Köhler, Nature 256 (1975), 495-7). For example, mice may be alternately im-

munized with human and non-chimpanzee primate cell surface antigen, such as PSMA. From these mice, cross-species specific antibody-producing hybridoma cells are isolated via hybridoma technology and analysed by FACS as set forth above. The generation and analysis of bispecific polypeptides such as bispecific single chain antibodies exhibiting cross-species specificity as described herein is shown in the following examples. The advantages of the bispecific single chain antibodies exhibiting cross-species specificity include the points enumerated herein.

[0081] It is particularly preferred for the bispecific single chain antibody molecule of the invention that the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 ϵ chain comprises a VL region comprising CDR-L1, CDR-L2 and CDR-L3 selected from:

- (a) CDR-L1 as depicted in SEQ ID NO. 27, CDR-L2 as depicted in SEQ ID NO. 28 and CDR-L3 as depicted in SEQ ID NO. 29;
- (b) CDR-L1 as depicted in SEQ ID NO. 117, CDR-L2 as depicted in SEQ ID NO. 118 and CDR-L3 as depicted in SEQ ID NO. 119; and
- (c) CDR-L1 as depicted in SEQ ID NO. 153, CDR-L2 as depicted in SEQ ID NO. 154 and CDR-L3 as depicted in SEQ ID NO. 155.

[0082] The variable regions, i.e. the variable light chain ("L" or "VL") and the variable heavy chain ("H" or "VH") are understood in the art to provide the binding domain of an antibody. This variable regions harbor the complementary determining regions.

[0083] The term "complementary determining region" (CDR) is well known in the art to dictate the antigen specificity of an antibody. The term "CDR-L" or "L CDR" or "LCDR" refers to CDRs in the VL, whereas the term "CDR-H" or "H CDR" or "HCDR" refers to the CDRs in the VH.

[0084] In an alternatively preferred embodiment of the bispecific single chain antibody molecule of the invention the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 ϵ chain comprises a VH region comprising CDR-H 1, CDR-H2 and CDR-H3 selected from:

- (a) CDR-H1 as depicted in SEQ ID NO. 12, CDR-H2 as depicted in SEQ ID NO. 13 and CDR-H3 as depicted in SEQ ID NO. 14;
- (b) CDR-H1 as depicted in SEQ ID NO. 30, CDR-H2 as depicted in SEQ ID NO. 31 and CDR-H3 as depicted in SEQ ID NO. 32;
- (c) CDR-H1 as depicted in SEQ ID NO. 48, CDR-H2 as depicted in SEQ ID NO. 49 and CDR-H3 as depicted in SEQ ID NO. 50;
- (d) CDR-H1 as depicted in SEQ ID NO. 66, CDR-H2 as depicted in SEQ ID NO. 67 and CDR-H3 as depicted in SEQ ID NO. 68;
- (e) CDR-H1 as depicted in SEQ ID NO. 84, CDR-H2 as depicted in SEQ ID NO. 85 and CDR-H3 as depicted in SEQ ID NO. 86;
- (f) CDR-H1 as depicted in SEQ ID NO. 102, CDR-H2 as depicted in SEQ ID NO. 103 and CDR-H3 as depicted in SEQ ID NO. 104;
- (g) CDR-H1 as depicted in SEQ ID NO. 120, CDR-H2 as depicted in SEQ ID NO. 121 and CDR-H3 as depicted in SEQ ID NO. 122;
- (h) CDR-H1 as depicted in SEQ ID NO. 138, CDR-H2 as depicted in SEQ ID NO. 139 and CDR-H3 as depicted in SEQ ID NO. 140;
- (i) CDR-H1 as depicted in SEQ ID NO. 156, CDR-H2 as depicted in SEQ ID NO. 157 and CDR-H3 as depicted in SEQ ID NO. 158; and
- (j) CDR-H1 as depicted in SEQ ID NO. 174, CDR-H2 as depicted in SEQ ID NO. 175 and CDR-H3 as depicted in SEQ ID NO. 176.

[0085] It is further preferred that the binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 ϵ chain comprises a VL region selected from the group consisting of a VL region as depicted in SEQ ID NO. 35, 39, 125, 129, 161 or 165.

[0086] It is alternatively preferred that the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 ϵ chain comprises a VH region selected from the group consisting of a VH region as depicted in SEQ ID NO. 15, 19, 33, 37, 51, 55, 69, 73, 87, 91, 105, 109, 123, 127, 141, 145, 159, 163, 177 or 181.

[0087] More preferably, the bispecific single chain antibody molecule of the invention is characterized by the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 ϵ chain, which comprises a VL region and a VH region selected from the group consisting of:

- (a) a VL region as depicted in SEQ ID NO. 17 or 21 and a VH region as depicted in SEQ ID NO. 15 or 19;

- (b) a VL region as depicted in SEQ ID NO. 35 or 39 and a VH region as depicted in SEQ ID NO. 33 or 37;
- (c) a VL region as depicted in SEQ ID NO. 53 or 57 and a VH region as depicted in SEQ ID NO. 51 or 55;
- (d) a VL region as depicted in SEQ ID NO. 71 or 75 and a VH region as depicted in SEQ ID NO. 69 or 73;
- (e) a VL region as depicted in SEQ ID NO. 89 or 93 and a VH region as depicted in SEQ ID NO. 87 or 91;
- (f) a VL region as depicted in SEQ ID NO. 107 or 111 and a VH region as depicted in SEQ ID NO. 105 or 109;
- (g) a VL region as depicted in SEQ ID NO. 125 or 129 and a VH region as depicted in SEQ ID NO. 123 or 127;
- (h) a VL region as depicted in SEQ ID NO. 143 or 147 and a VH region as depicted in SEQ ID NO. 141 or 145;
- (i) a VL region as depicted in SEQ ID NO. 161 or 165 and a VH region as depicted in SEQ ID NO. 159 or 163; and
- (j) a VL region as depicted in SEQ ID NO. 179 or 183 and a VH region as depicted in SEQ ID NO. 177 or 181.

[0088] According to a preferred embodiment of the bispecific single chain antibody molecule of the invention the pairs of VH-regions and VL-regions in the first binding domain binding to CD3 epsilon are in the format of a single chain antibody (scFv). The VH and VL regions are arranged in the order VH-VL or VL-VH. It is preferred that the VH-region is positioned N-terminally to a linker sequence. The VL-region is positioned C-terminally of the linker sequence. Put in other words, the domain arrangement in the CD3 binding domain of the bispecific single chain antibody molecule of the invention is preferably VH-VL, with said CD3 binding domain located C-terminally to the second (cell surface antigen, such as PSMA) binding domain. Preferably the VH-VL comprises or is SEQ ID NO. 185.

[0089] A preferred embodiment of the above described bispecific single chain antibody molecule of the invention is characterized by the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 epsilon chain comprising an amino acid sequence selected from the group consisting of SEQ ID NOS: 23, 25, 41, 43, 59, 61, 77, 79, 95, 97, 113, 115, 131, 133, 149, 151, 167, 169, 185 or 187.

[0090] The invention further relates to an above described bispecific single chain antibody, wherein the second binding domain binds to the cell surface antigen PSMA.

[0091] According to a preferred embodiment of the invention an above characterized bispecific single chain antibody molecule comprises a group of the following sequences as CDR H1, CDR H2, CDR H3, CDR L1, CDR L2 and CDR L3 in the second binding domain selected from the group consisting of:

- a) CDR H1-3 of SEQ ID NO: 394 - 396 and CDR L1-3 of SEQ ID NO: 389 - 391;
- b) CDR H1-3 of SEQ ID NO: 408 - 410 and CDR L1-3 of SEQ ID NO: 403 - 405;
- c) CDR H1-3 of SEQ ID NO: 422 - 424 and CDR L1-3 of SEQ ID NO: 417 - 419;
- d) CDR H1-3 of SEQ ID NO: 436 - 438 and CDR L1-3 of SEQ ID NO: 431 - 433;
- e) CDR H1-3 of SEQ ID NO: 445 - 447 and CDR L1-3 of SEQ ID NO: 450 - 452;
- f) CDR H1-3 of SEQ ID NO: 464 - 466 and CDR L1-3 of SEQ ID NO: 459 - 461;
- g) CDR H1-3 of SEQ ID NO: 478 - 480 and CDR L1-3 of SEQ ID NO: 473 - 475;
- h) CDR H1-3 of SEQ ID NO: 492 - 494 and CDR L1-3 of SEQ ID NO: 487 - 489;
- i) CDR H1-3 of SEQ ID NO: 506 - 508 and CDR L1-3 of SEQ ID NO: 501 - 503;
- j) CDR H1-3 of SEQ ID NO: 520 - 522 and CDR L1-3 of SEQ ID NO: 515 - 517;
- k) CDR H1-3 of SEQ ID NO: 534 - 536 and CDR L1-3 of SEQ ID NO: 529 - 531;
- l) CDR H1-3 of SEQ ID NO: 548 - 550 and CDR L1-3 of SEQ ID NO: 543 - 545;
- m) CDR H1-3 of SEQ ID NO: 562 - 564 and CDR L1-3 of SEQ ID NO: 557 - 559;
- n) CDR H1-3 of SEQ ID NO: 576 - 578 and CDR L1-3 of SEQ ID NO: 571 - 573;
- o) CDR H1-3 of SEQ ID NO: 590 - 592 and CDR L1-3 of SEQ ID NO: 585 - 587;
- p) CDR H1-3 of SEQ ID NO: 604 - 606 and CDR L1-3 of SEQ ID NO: 599 - 601;
- q) CDR H1-3 of SEQ ID NO: 618 - 620 and CDR L1-3 of SEQ ID NO: 613 - 615;
- r) CDR H1-3 of SEQ ID NO: 632 - 634 and CDR L1-3 of SEQ ID NO: 627 - 629;
- s) CDR H1-3 of SEQ ID NO: 646 - 648 and CDR L1-3 of SEQ ID NO: 641 - 643;
- t) CDR H1-3 of SEQ ID NO: 660 - 662 and CDR L1-3 of SEQ ID NO: 655 - 657;
- u) CDR H1-3 of SEQ ID NO: 674 - 676 and CDR L1-3 of SEQ ID NO: 669 - 671;
- v) CDR H1-3 of SEQ ID NO: 688 - 690 and CDR L1-3 of SEQ ID NO: 683 - 685;
- w) CDR H1-3 of SEQ ID NO: 702 - 704 and CDR L1-3 of SEQ ID NO: 697 - 699;
- x) CDR H1-3 of SEQ ID NO: 716 - 718 and CDR L1-3 of SEQ ID NO: 711 - 713; and
- y) CDR H1-3 of SEQ ID NO: 729 - 731 and CDR L1-3 of SEQ ID NO: 724 - 726.

[0092] The sequences of the corresponding VL- and VH-regions of the second binding domain of the bispecific single chain antibody molecule of the invention as well as of the respective scFvs are shown in the sequence listing.

[0093] In the bispecific single chain antibody molecule of the invention the binding domains are arranged in the order VL-VH-VH-VL, VL-VH-VL-VH, VH-VL-VH-VL or VH-VL-VL-VH, as exemplified in the appended examples. Preferably, the binding domains are arranged in the order VH PSMA-VL PSMA-VH CD3-VL CD3 or VL PSMA-VH PSMA-VH CD3-

VL CD3.

[0094] A particularly preferred embodiment of the invention concerns an above characterized polypeptide, wherein the bispecific single chain antibody molecule comprises a sequence selected from:

(a) an amino acid sequence as depicted in any of SEQ ID NOs: 399, 413, 427, 441, 455, 469, 483, 497, 511, 525, 539, 553, 567, 581, 595, 609, 623, 637, 651, 665, 679, 693, 707, 721, 734, 799, 817, 863, 849, 835, 785, 899, 935, 1017, 1031, 917, 1003, 953, 971 or 989;

(b) an amino acid sequence encoded by a nucleic acid sequence as depicted in any of SEQ ID NOs: 400, 414, 428, 442, 456, 470, 484, 498, 512, 526, 540, 554, 568, 582, 596, 610, 624, 638, 652, 666, 680, 694, 708, 736 735, 800, 818, 864, 850, 836, 786, 882, 900, 936, 1018, 1032, 918, 1004, 954, 972, 990, 804, 822, 868, 886, 904, 940, 922, 958 or 976;

(c) an amino acid sequence at least 90 % identical, more preferred at least 95 % identical, most preferred at least 96 % identical to the amino acid sequence of (a) or (b).

[0095] The invention relates to a bispecific single chain antibody molecule comprising an amino acid sequence as depicted in any of SEQ ID NOs: 399, 413, 427, 441, 455, 469, 483, 497, 511, 525, 539, 553, 567, 581, 595, 609, 623, 637, 651, 665, 679, 693, 707, 721, 734, 799, 817, 863, 849, 835, 785, 899, 935, 1017, 1031, 917, 1003, 953, 971 or 989, as well as to amino acid sequences at least 85% identical, preferably 90 %, more preferred at least 95 % identical, most preferred at least 96, 97, 98, or 99 % identical to the amino acid sequence of SEQ ID NOs: 399, 413, 427, 441, 455, 469, 483, 497, 511, 525, 539, 553, 567, 581, 595, 609, 623, 637, 651, 665, 679, 693, 707, 721, 734, 799, 817, 863, 849, 835, 785, 899, 935, 1017, 1031, 917, 1003, 953, 971 or 989. The invention relates also to the corresponding nucleic acid sequences as depicted in any of SEQ ID NOs: 400, 414, 428, 442, 456, 470, 484, 498, 512, 526, 540, 554, 568, 582, 596, 610, 624, 638, 652, 666, 680, 694, 708, 736 735, 800, 818, 864, 850, 836, 786, 882, 900, 936, 1018, 1032, 918, 1004, 954, 972, 990, 804, 822, 868, 886, 904, 940, 922, 958 or 976 as well as to nucleic acid sequences at least 85% identical, preferably 90 %, more preferred at least 95 % identical, most preferred at least 96, 97, 98, or 99 % identical to the nucleic acid sequences shown in SEQ ID NOs: 400, 414, 428, 442, 456, 470, 484, 498, 512, 526, 540, 554, 568, 582, 596, 610, 624, 638, 652, 666, 680, 694, 708, 736, 735, 800, 818, 864, 850, 836, 786, 882, 900, 936, 1018, 1032, 918, 1004, 954, 972, 990, 804, 822, 868, 886, 904, 940, 922, 958 or 976. It is to be understood that the sequence identity is determined over the entire nucleotide or amino acid sequence. For sequence alignments, for example, the programs Gap or BestFit can be used (Needleman and Wunsch J. Mol. Biol. 48 (1970), 443-453; Smith and Waterman, Adv. Appl. Math 2 (1981), 482-489), which is contained in the GCG software package (Genetics Computer Group, 575 Science Drive, Madison, Wisconsin, USA 53711 (1991)). It is a routine method for those skilled in the art to determine and identify a nucleotide or amino acid sequence having e.g. 85% (90%, 95%, 96%, 97%, 98% or 99%) sequence identity to the nucleotide or amino acid sequences of the bispecific single chain antibody of the invention by using e.g. one of the above mentioned programs. For example, according to Crick's Wobble hypothesis, the 5' base on the anti-codon is not as spatially confined as the other two bases, and could thus have non-standard base pairing. Put in other words: the third position in a codon triplet may vary so that two triplets which differ in this third position may encode the same amino acid residue. Said hypothesis is well known to the person skilled in the art (see e.g. http://en.wikipedia.org/wiki/Wobble_Hypothesis; Crick, J Mol Biol 19 (1966): 548-55).

[0096] Preferred domain arrangements in the PSMAxCD3 bispecific single chain antibody constructs of the invention are shown in the following examples.

[0097] In a preferred embodiment of the invention, the bispecific single chain antibodies are cross-species specific for CD3 epsilon and for the human and non-chimpanzee primate cell surface antigen PSMA, recognized by their second binding domain.

[0098] In an alternative embodiment the present invention provides a nucleic acid sequence encoding an above described bispecific single chain antibody molecule of the invention.

[0099] The present invention also relates to a vector comprising the nucleic acid molecule of the present invention.

[0100] Many suitable vectors are known to those skilled in molecular biology, the choice of which would depend on the function desired and include plasmids, cosmids, viruses, bacteriophages and other vectors used conventionally in genetic engineering. Methods which are well known to those skilled in the art can be used to construct various plasmids and vectors; see, for example, the techniques described in Sambrook et al. (loc cit.) and Ausubel, Current Protocols in Molecular Biology, Green Publishing Associates and Wiley Interscience, N.Y. (1989), (1994). Alternatively, the polynucleotides and vectors of the invention can be reconstituted into liposomes for delivery to target cells. As discussed in further details below, a cloning vector was used to isolate individual sequences of DNA. Relevant sequences can be transferred into expression vectors where expression of a particular polypeptide is required. Typical cloning vectors include pBluescript SK, pGEM, pUC9, pBR322 and pGBT9. Typical expression vectors include pTRE, pCAL-n-EK, pESP-1, pOP13CAT.

[0101] Preferably said vector comprises a nucleic acid sequence which is a regulatory sequence operably linked to

said nucleic acid sequence defined herein.

[0102] The term "regulatory sequence" refers to DNA sequences, which are necessary to effect the expression of coding sequences to which they are ligated. The nature of such control sequences differs depending upon the host organism. In prokaryotes, control sequences generally include promoter, ribosomal binding site, and terminators. In eukaryotes generally control sequences include promoters, terminators and, in some instances, enhancers, transactivators or transcription factors. The term "control sequence" is intended to include, at a minimum, all components the presence of which are necessary for expression, and may also include additional advantageous components.

[0103] The term "operably linked" refers to a juxtaposition wherein the components so described are in a relationship permitting them to function in their intended manner. A control sequence "operably linked" to a coding sequence is ligated in such a way that expression of the coding sequence is achieved under conditions compatible with the control sequences. In case the control sequence is a promoter, it is obvious for a skilled person that double-stranded nucleic acid is preferably used.

[0104] Thus, the recited vector is preferably an expression vector. An "expression vector" is a construct that can be used to transform a selected host and provides for expression of a coding sequence in the selected host. Expression vectors can for instance be cloning vectors, binary vectors or integrating vectors. Expression comprises transcription of the nucleic acid molecule preferably into a translatable mRNA.

[0105] Regulatory elements ensuring expression in prokaryotes and/or eukaryotic cells are well known to those skilled in the art. In the case of eukaryotic cells they comprise normally promoters ensuring initiation of transcription and optionally poly-A signals ensuring termination of transcription and stabilization of the transcript. Possible regulatory elements permitting expression in prokaryotic host cells comprise, e.g., the P_L, *lac*, *trp* or *tac* promoter in *E. coli*, and examples of regulatory elements permitting expression in eukaryotic host cells are the AOX1 or GAL1 promoter in yeast or the CMV-, SV40-, RSV-promoter (Rous sarcoma virus), CMV-enhancer, SV40-enhancer or a globin intron in mammalian and other animal cells.

[0106] Beside elements, which are responsible for the initiation of transcription such regulatory elements may also comprise transcription termination signals, such as the SV40-poly-A site or the tk-poly-A site, downstream of the polynucleotide. Furthermore, depending on the expression system used leader sequences capable of directing the polypeptide to a cellular compartment or secreting it into the medium may be added to the coding sequence of the recited nucleic acid sequence and are well known in the art; see also the appended Examples. The leader sequence(s) is (are) assembled in appropriate phase with translation, initiation and termination sequences, and preferably, a leader sequence capable of directing secretion of translated protein, or a portion thereof, into the periplasmic space or extracellular medium. Optionally, the heterologous sequence can encode a fusion protein including an N-terminal identification peptide imparting desired characteristics, e.g., stabilization or simplified purification of expressed recombinant product; see supra. In this context, suitable expression vectors are known in the art such as Okayama-Berg cDNA expression vector pcDV1 (Pharmacia), pCDM8, pRc/CMV, pcDNA1, pcDNA3 (In-vitro gene), pEF-DHFR, pEF-ADA or pEF-neo (Mack et al. PNAS (1995) 92, 7021-7025 and Raum et al. Cancer Immunol Immunother (2001) 50(3), 141-150) or pSPORT1 (GIBCO BRL).

[0107] Preferably, the expression control sequences will be eukaryotic promoter systems in vectors capable of transforming of transfecting eukaryotic host cells, but control sequences for prokaryotic hosts may also be used. Once the vector has been incorporated into the appropriate host, the host is maintained under conditions suitable for high level expression of the nucleotide sequences, and as desired, the collection and purification of the bispecific single chain antibody molecule of the invention may follow; see, e.g., the appended examples.

[0108] An alternative expression system, which can be used to express a cell cycle interacting protein is an insect system. In one such system, *Autographa californica* nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia* larvae. The coding sequence of a recited nucleic acid molecule may be cloned into a nonessential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of said coding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein coat. The recombinant viruses are then used to infect *S. frugiperda* cells or *Trichoplusia* larvae in which the protein of the invention is expressed (Smith, J. Virol. 46 (1983), 584; Engelhard, Proc. Nat. Acad. Sci. USA 91 (1994), 3224-3227).

[0109] Additional regulatory elements may include transcriptional as well as translational enhancers. Advantageously, the above-described vectors of the invention comprise a selectable and/or scorable marker.

[0110] Selectable marker genes useful for the selection of transformed cells and, e.g., plant tissue and plants are well known to those skilled in the art and comprise, for example, antimetabolite resistance as the basis of selection for dhfr, which confers resistance to methotrexate (Reiss, Plant Physiol. (Life Sci. Adv.) 13 (1994), 143-149); npt, which confers resistance to the aminoglycosides neomycin, kanamycin and paromycin (Herrera-Estrella, EMBO J. 2 (1983), 987-995) and hygromycin (Marsh, Gene 32 (1984), 481-485). Additional selectable genes have been described, namely trpB, which allows cells to utilize indole in place of tryptophan; hisD, which allows cells to utilize histidine (Hartman, Proc. Natl. Acad. Sci. USA 85 (1988), 8047); mannose-6-phosphate isomerase which allows cells to utilize mannose (WO 94/20627) and ODC (ornithine decarboxylase) which confers resistance to

the ornithine decarboxylase inhibitor, 2-(difluoromethyl)-DL-ornithine, DFMO (McConlogue, 1987, In: Current Communications in Molecular Biology, Cold Spring Harbor Laboratory ed.) or deaminase from *Aspergillus terreus* which confers resistance to Blasticidin S (Tamura, Biosci. Biotechnol. Biochem. 59 (1995), 2336-2338).

[0111] Useful scorable markers are also known to those skilled in the art and are commercially available. Advantageously, said marker is a gene encoding luciferase (Giacomin, Pl. Sci. 116 (1996), 59-72; Scikantha, J. Bact. 178 (1996), 121), green fluorescent protein (Gerdes, FEBS Lett. 389 (1996), 44-47) or β -glucuronidase (Jefferson, EMBO J. 6 (1987), 3901-3907). This embodiment is particularly useful for simple and rapid screening of cells, tissues and organisms containing a recited vector.

[0112] As described above, the recited nucleic acid molecule can be used alone or as part of a vector to express the bispecific single chain antibody molecule of the invention in cells, for, e.g., purification but also for gene therapy purposes. The nucleic acid molecules or vectors containing the DNA sequence(s) encoding any one of the above described bispecific single chain antibody molecule of the invention is introduced into the cells which in turn produce the polypeptide of interest. Gene therapy, which is based on introducing therapeutic genes into cells by ex-vivo or in-vivo techniques is one of the most important applications of gene transfer. Suitable vectors, methods or gene-delivery systems for in-vitro or in-vivo gene therapy are described in the literature and are known to the person skilled in the art; see, e.g., Giordano, Nature Medicine 2 (1996), 534-539; Schaper, Circ. Res. 79 (1996), 911-919; Anderson, Science 256 (1992), 808-813; Verma, Nature 389 (1994), 239; Isner, Lancet 348 (1996), 370-374; Muhlhauser, Circ. Res. 77 (1995), 1077-1086; Onodera, Blood 91 (1998), 30-36; Verma, Gene Ther. 5 (1998), 692-699; Nabel, Ann. N.Y. Acad. Sci. 811 (1997), 289-292; Verzeletti, Hum. Gene Ther. 9 (1998), 2243-51; Wang, Nature Medicine 2 (1996), 714-716; WO 94/29469; WO 97/00957, US 5,580,859; US 5,589,466; or Schaper, Current Opinion in Biotechnology 7 (1996), 635-640; dos Santos Coura and Nardi Virol J. (2007), 4:99. The recited nucleic acid molecules and vectors may be designed for direct introduction or for introduction via liposomes, or viral vectors (e.g., adenoviral, retroviral) into the cell. Preferably, said cell is a germ line cell, embryonic cell, or egg cell or derived there from, most preferably said cell is a stem cell. An example for an embryonic stem cell can be, inter alia, a stem cell as described in Nagy, Proc. Natl. Acad. Sci. USA 90 (1993), 8424-8428.

[0113] The invention also provides for a host transformed or transfected with a vector of the invention. Said host may be produced by introducing the above described vector of the invention or the above described nucleic acid molecule of the invention into the host. The presence of at least one vector or at least one nucleic acid molecule in the host may mediate the expression of a gene encoding the above described single chain antibody constructs.

[0114] The described nucleic acid molecule or vector of the invention, which is introduced in the host may either integrate into the genome of the host or it may be maintained extrachromosomally.

[0115] The host can be any prokaryote or eukaryotic cell.

[0116] The term "prokaryote" is meant to include all bacteria, which can be transformed or transfected with DNA or RNA molecules for the expression of a protein of the invention. Prokaryotic hosts may include gram negative as well as gram positive bacteria such as, for example, *E. coli*, *S. typhimurium*, *Serratia marcescens* and *Bacillus subtilis*. The term "eukaryotic" is meant to include yeast, higher plant, insect and preferably mammalian cells. Depending upon the host employed in a recombinant production procedure, the protein encoded by the polynucleotide of the present invention may be glycosylated or may be non-glycosylated. Especially preferred is the use of a plasmid or a virus containing the coding sequence of the bispecific single chain antibody molecule of the invention and genetically fused thereto an N-terminal FLAG-tag and/or C-terminal His-tag. Preferably, the length of said FLAG-tag is about 4 to 8 amino acids, most preferably 8 amino acids. An above described polynucleotide can be used to transform or transfect the host using any of the techniques commonly known to those of ordinary skill in the art. Furthermore, methods for preparing fused, operably linked genes and expressing them in, e.g., mammalian cells and bacteria are well-known in the art (Sambrook, loc cit.).

[0117] Preferably, said the host is a bacterium or an insect, fungal, plant or animal cell.

[0118] It is particularly envisaged that the recited host may be a mammalian cell. Particularly preferred host cells comprise CHO cells, COS cells, myeloma cell lines like SP2/0 or NS/0. As illustrated in the appended examples, particularly preferred are CHO-cells as hosts.

[0119] More preferably said host cell is a human cell or human cell line, e.g. per.c6 (Kroos, Biotechnol. Prog., 2003, 19:163-168).

[0120] In a further embodiment, the present invention thus relates to a process for the production of a bispecific single chain antibody molecule of the invention, said process comprising culturing a host of the invention under conditions allowing the expression of the bispecific single chain antibody molecule of the invention and recovering the produced polypeptide from the culture.

[0121] The transformed hosts can be grown in fermentors and cultured according to techniques known in the art to achieve optimal cell growth. The bispecific single chain antibody molecule of the invention can then be isolated from the growth medium, cellular lysates, or cellular membrane fractions. The isolation and purification of the, e.g., microbially expressed bispecific single chain antibody molecules may be by any conventional means such as, for example, preparative chromatographic separations and immunological separations such as those involving the use of monoclonal or

polyclonal antibodies directed, e.g., against a tag of the bispecific single chain antibody molecule of the invention or as described in the appended examples.

[0122] The conditions for the culturing of a host, which allow the expression are known in the art to depend on the host system and the expression system/vector used in such process. The parameters to be modified in order to achieve conditions allowing the expression of a recombinant polypeptide are known in the art. Thus, suitable conditions can be determined by the person skilled in the art in the absence of further inventive input.

[0123] Once expressed, the bispecific single chain antibody molecule of the invention can be purified according to standard procedures of the art, including ammonium sulfate precipitation, affinity columns, column chromatography, gel electrophoresis and the like; see, Scopes, "Protein Purification", Springer-Verlag, N.Y. (1982). Substantially pure polypeptides of at least about 90 to 95% homogeneity are preferred, and 98 to 99% or more homogeneity are most preferred, for pharmaceutical uses. Once purified, partially or to homogeneity as desired, the bispecific single chain antibody molecule of the invention may then be used therapeutically (including extracorporeally) or in developing and performing assay procedures. Furthermore, examples for methods for the recovery of the bispecific single chain antibody molecule of the invention from a culture are described in detail in the appended examples. The recovery can also be achieved by a method for the isolation of the bispecific single chain antibody molecule of the invention capable of binding to an epitope of human and non-chimpanzee primate CD3 ϵ (CD3 ϵ , the method comprising the steps of:

- (a) contacting the polypeptide(s) with an N-terminal fragment of the extracellular domain of CD3 ϵ of maximal 27 amino acids comprising the amino acid sequence Gln-Asp-Gly-Asn-Glu-Glu-Met-Gly (SEQ ID NO. 341) or Gln-Asp-Gly-Asn-Glu-Glu-Ile-Gly (SEQ ID NO. 342), fixed via its C-terminus to a solid phase;
- (b) eluting the bound polypeptide(s) from said fragment; and
- (c) isolating the polypeptide(s) from the eluate of (b).

[0124] It is preferred that the polypeptide(s) isolated by the above method of the invention are of human origin.

[0125] This method or the isolation of the bispecific single chain antibody molecule of the invention is understood as a method for the isolation of one or more different polypeptides with the same specificity for the fragment of the extracellular domain of CD3 ϵ comprising at its N-terminus the amino acid sequence Gln-Asp-Gly-Asn-Glu-Glu-Met-Gly (SEQ ID NO. 341) or Gln-Asp-Gly-Asn-Glu-Glu-Ile-Gly (SEQ ID NO. 342) from a plurality of polypeptide candidates as well as a method for the purification of a polypeptide from a solution. A non-limiting example for the latter method for the purification of a bispecific single chain antibody molecule from a solution is e.g. the purification of a recombinantly expressed bispecific single chain antibody molecule from a culture supernatant or a preparation from such culture.

[0126] As stated above the fragment used in this method is an N-terminal fragment of the extracellular domain of the primate CD3 ϵ molecule. The amino acid sequence of the extracellular domain of the CD3 ϵ molecule of different species is depicted in SEQ ID NOs: 1, 3, 5 and 7. The two forms of the N-terminal octamer are depicted in SEQ ID NOs: 341 and 342. It is preferred that this N-terminus is freely available for binding of the polypeptides to be identified by the method of the invention. The term "freely available" is understood in the context of the invention as free of additional motives such as a His-tag. The interference of such a His-tag with a binding molecule identified by the method of the invention is described in the appended Examples 6 and 20.

[0127] According to this method said fragment is fixed via its C-terminus to a solid phase. The person skilled in the art will easily and without any inventive ado elect a suitable solid phase support dependent from the used embodiment of the method of the invention. Examples for a solid support comprise but are not limited to matrices like beads (e.g. agarose beads, sepharose beads, polystyrol beads, dextran beads), plates (culture plates or MultiWell plates) as well as chips known e.g. from Biacore[®]. The selection of the means and methods for the fixation/immobilization of the fragment to said solid support depend on the election of the solid support. A commonly used method for the fixation/immobilization is a coupling via an N-hydroxysuccinimide (NHS) ester. The chemistry underlying this coupling as well as alternative methods for the fixation/immobilization are known to the person skilled in the art, e.g. from Hermanson "Bioconjugate Techniques", Academic Press, Inc. (1996). For the fixation to/immobilization on chromatographic supports the following means are commonly used: NHS-activated sepharose (e.g. HiTrap-NHS of GE Life Science-Amersham), CnBr-activated sepharose (e.g. GE Life Science-Amersham), NHS-activated dextran beads (Sigma) or activated polymethacrylate. These reagents may also be used in a batch approach. Moreover, dextran beads comprising iron oxide (e.g. available from Miltenyi) may be used in a batch approach. These beads may be used in combination with a magnet for the separation of the beads from a solution. Polypeptides can be immobilized on a Biacore chip (e.g. CM5 chips) by the use of NHS activated carboxymethyldextran. Further examples for an appropriate solid support are amine reactive MultiWell plates (e.g. Nunc Immobilizer[™] plates). According to this method said fragment of the extracellular domain of CD3 epsilon can be directly coupled to the solid support or via a stretch of amino acids, which might be a linker or another protein/polypeptide moiety. Alternatively, the extracellular domain of CD3 epsilon can be indirectly coupled via one or more adaptor molecule(s).

[0128] Means and methods for the elution of a peptide or polypeptide bound to an immobilized epitope are well known

in the art. The same holds true for methods for the isolation of the identified polypeptide(s) from the eluate.

[0129] A method for the isolation of one or more different bispecific single chain antibody molecule(s) with the same specificity for the fragment of the extracellular domain of CD3 ϵ comprising at its N-terminus the amino acid sequence Gln-Asp-Gly-Asn-Glu-Glu-X-Gly (with X being Met or Ile) from a plurality of polypeptide candidates may comprise one

or more steps of the following methods for the selection of antigen-specific entities:

CD3 ϵ specific binding domains can be selected from antibody derived repertoires. A phage display library can be constructed based on standard procedures, as for example disclosed in "Phage Display: A Laboratory Manual"; Ed. Barbas, Burton, Scott & Silverman; Cold Spring Harbor Laboratory Press, 2001. The format of the antibody fragments in the antibody library can be scFv, but may generally also be a Fab fragment or even a single domain antibody fragment. For the isolation of antibody fragments naive antibody fragment libraries may be used. For the selection of potentially low immunogenic binding entities in later therapeutic use, human antibody fragment libraries may be favourable for the direct selection of human antibody fragments. In some cases they may form the basis for synthetic antibody libraries (Knappik et al. J Mol. Biol. 2000, 296:57 ff). The corresponding format may be Fab, scFv (as described below) or domain antibodies (dAbs, as reviewed in Holt et al., Trends Biotechnol. 2003, 21:484 ff).

[0130] It is also known in the art that in many cases there is no immune human antibody source available against the target antigen. Therefore animals are immunized with the target antigen and the respective antibody libraries isolated from animal tissue as e.g. spleen or PBMCs. The N-terminal fragment may be biotinylated or covalently linked to proteins like KLH or bovine serum albumin (BSA). According to common approaches rodents are used for immunization. Some immune antibody repertoires of non-human origin may be especially favourable for other reasons, e.g. for the presence of single domain antibodies (VHH) derived from cameloid species (as described in Muyldermans, J Biotechnol. 74:277; De Genst et al. Dev Comp Immunol. 2006, 30:187 ff). Therefore a corresponding format of the antibody library may be Fab, scFv (as described below) or single domain antibodies (VHH).

[0131] In one possible approach ten weeks old F1 mice from balb/c x C57black crossings can be immunized with whole cells e.g. expressing transmembrane EpCAM N-terminally displaying as translational fusion the N-terminal amino acids 1 to 27 of the mature CD3 ϵ chain. Alternatively, mice can be immunized with 1-27 CD3 epsilon-Fc fusion protein (a corresponding approach is described in the appended Example 2). After booster immunization(s), blood samples can be taken and antibody serum titer against the CD3-positive T cells can be tested e.g. in FACS analysis. Usually, serum titers are significantly higher in immunized than in non-immunized animals.

[0132] Immunized animals may form the basis for the construction of immune antibody libraries. Examples of such libraries comprise phage display libraries. Such libraries may be generally constructed based on standard procedures, as for example disclosed in "Phage Display: A Laboratory Manual"; Ed. Barbas, Burton, Scott & Silverman; Cold Spring Harbor Laboratory Press, 2001.

[0133] The non-human antibodies can also be humanized via phage display due to the generation of more variable antibody libraries that can be subsequently enriched for binders during selection.

[0134] In a phage display approach any one of the pools of phages that displays the antibody libraries forms a basis to select binding entities using the respective antigen as target molecule. The central step in which antigen specific, antigen bound phages are isolated is designated as panning. Due to the display of the antibody fragments on the surface of the phages, this general method is called phage display. One preferred method of selection is the use of small proteins such as the filamentous phage N2 domain translationally fused to the N-terminus of the scFv displayed by the phage. Another display method known in the art, which may be used to isolate binding entities is the ribosome display method (reviewed in Groves & Osbourn, Expert Opin Biol Ther. 2005, 5:125 ff; Lipovsek & Pluckthun, J Immunol Methods 2004, 290:52 ff). In order to demonstrate binding of scFv phage particles to a 1-27 CD3 ϵ -Fc fusion protein a phage library carrying the cloned scFv-repertoire can be harvested from the respective culture supernatant by PEG (polyethyleneglycole). ScFv phage particles may be incubated with immobilized CD3 ϵ Fc fusion protein. The immobilized CD3 ϵ Fc fusion protein may be coated to a solid phase. Binding entities can be eluted and the eluate can be used for infection of fresh uninfected bacterial hosts. Bacterial hosts successfully transduced with a phagemid copy, encoding a human scFv-fragment, can be selected again for carbenicillin resistance and subsequently infected with e.g. VCMS 13 helper phage to start the second round of antibody display and in vitro selection. A total of 4 to 5 rounds of selections is carried out, normally. The binding of isolated binding entities can be tested on CD3 epsilon positive Jurkat cells, HPBALL cells, PBMCs or transfected eukaryotic cells that carry the N-terminal CD3 ϵ sequence fused to surface displayed EpCAM using a flow cytometric assay (see appended Example 4).

[0135] Preferably, the above method may be a method, wherein the fragment of the extracellular domain of CD3 ϵ consists of one or more fragments of a polypeptide having an amino acid sequence of any one depicted in SEQ ID NOs. 2, 4, 6 or 8. More preferably, said fragment is 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27 amino acid residues in length.

[0136] This method of identification of a bispecific single chain antibody molecule may be a method of screening a plurality of bispecific single chain antibody molecules comprising a cross-species specific binding domain binding to an epitope of human and non-chimpanzee primate CD3 ϵ . Alternatively, the method of identification is a method of purifi-

cation/isolation of a bispecific single chain antibody molecule comprising a cross-species specific binding domain binding to an epitope of human and non-chimpanzee primate CD3ε.

[0137] Furthermore, the invention provides for a composition comprising a bispecific single chain antibody molecule of the invention or a bispecific single chain antibody as produced by the process disclosed above. Preferably, said composition is a pharmaceutical composition.

[0138] The invention provides also for a bispecific single chain antibody molecule as defined herein, or produced according to the process as defined herein, wherein said bispecific single chain antibody molecule is for use in the prevention, treatment or amelioration of cancer. Preferably, said cancer is a solid tumor, more preferably a carcinoma or prostate cancer. It is preferred that the bispecific single chain is further comprising suitable formulations of carriers, stabilizers and/or excipients. Moreover, it is preferred that said bispecific single chain antibody molecule is suitable to be administered in combination with an additional drug. Said drug may be a non-proteinaceous compound or a proteinaceous compound and may be administered simultaneously or non-simultaneously with the bispecific single chain antibody molecule as defined herein.

[0139] In accordance with the invention, the term "pharmaceutical composition" relates to a composition for administration to a patient, preferably a human patient. The particular preferred pharmaceutical composition of this invention comprises bispecific single chain antibodies directed against and generated against context-independent CD3 epitopes. Preferably, the pharmaceutical composition comprises suitable formulations of carriers, stabilizers and/or excipients. In a preferred embodiment, the pharmaceutical composition comprises a composition for parenteral, transdermal, intraluminal, intraarterial, intrathecal and/or intranasal administration or by direct injection into tissue. It is in particular envisaged that said composition is administered to a patient via infusion or injection. Administration of the suitable compositions may be effected by different ways, e.g., by intravenous, intraperitoneal, subcutaneous, intramuscular, topical or intradermal administration. In particular, the present invention provides for an uninterrupted administration of the suitable composition. As a non-limiting example, uninterrupted, i.e. continuous administration may be realized by a small pump system worn by the patient for metering the influx of therapeutic agent into the body of the patient. The pharmaceutical composition comprising the bispecific single chain antibodies directed against and generated against context-independent CD3 epitopes of the invention can be administered by using said pump systems. Such pump systems are generally known in the art, and commonly rely on periodic exchange of cartridges containing the therapeutic agent to be infused. When exchanging the cartridge in such a pump system, a temporary interruption of the otherwise uninterrupted flow of therapeutic agent into the body of the patient may ensue. In such a case, the phase of administration prior to cartridge replacement and the phase of administration following cartridge replacement would still be considered within the meaning of the pharmaceutical means and methods of the invention together make up one "uninterrupted administration" of such therapeutic agent.

[0140] The continuous or uninterrupted administration of these bispecific single chain antibodies directed against and generated against context-independent CD3 epitopes of this invention may be intravenous or subcutaneous by way of a fluid delivery device or small pump system including a fluid driving mechanism for driving fluid out of a reservoir and an actuating mechanism for actuating the driving mechanism. Pump systems for subcutaneous administration may include a needle or a cannula for penetrating the skin of a patient and delivering the suitable composition into the patient's body. Said pump systems may be directly fixed or attached to the skin of the patient independently of a vein, artery or blood vessel, thereby allowing a direct contact between the pump system and the skin of the patient. The pump system can be attached to the skin of the patient for 24 hours up to several days. The pump system may be of small size with a reservoir for small volumes. As a non-limiting example, the volume of the reservoir for the suitable pharmaceutical composition to be administered can be between 0.1 and 50 ml.

[0141] The continuous administration may be transdermal by way of a patch worn on the skin and replaced at intervals. One of skill in the art is aware of patch systems for drug delivery suitable for this purpose. It is of note that transdermal administration is especially amenable to uninterrupted administration, as exchange of a first exhausted patch can advantageously be accomplished simultaneously with the placement of a new, second patch, for example on the surface of the skin immediately adjacent to the first exhausted patch and immediately prior to removal of the first exhausted patch. Issues of flow interruption or power cell failure do not arise.

[0142] The composition of the present invention, comprising in particular bispecific single chain antibodies directed against and generated against context-independent CD3 epitopes may further comprise a pharmaceutically acceptable carrier. Examples of suitable pharmaceutical carriers are well known in the art and include solutions, e.g. phosphate buffered saline solutions, water, emulsions, such as oil/water emulsions, various types of wetting agents, sterile solutions, liposomes, etc. Compositions comprising such carriers can be formulated by well known conventional methods. Formulations can comprise carbohydrates, buffer solutions, amino acids and/or surfactants. Carbohydrates may be non-reducing sugars, preferably trehalose, sucrose, octasulfate, sorbitol or xylitol. Such formulations may be used for continuous administrations which may be intravenous or subcutaneous with and/or without pump systems. Amino acids may be charged amino acids, preferably lysine, lysine acetate, arginine, glutamate and/or histidine. Surfactants may be detergents, preferably with a molecular weight of >1.2 KD and/or a polyether, preferably with a molecular weight of >3 KD.

Non-limiting examples for preferred detergents are Tween 20, Tween 40, Tween 60, Tween 80 or Tween 85. Non-limiting examples for preferred polyethers are PEG 3000, PEG 3350, PEG 4000 or PEG 5000. Buffer systems used in the present invention can have a preferred pH of 5-9 and may comprise citrate, succinate, phosphate, histidine and acetate. The compositions of the present invention can be administered to the subject at a suitable dose which can be determined e.g. by dose escalating studies by administration of increasing doses of the bispecific single chain antibody molecule of the invention exhibiting cross-species specificity described herein to non-chimpanzee primates, for instance macaques. As set forth above, the bispecific single chain antibody molecule of the invention exhibiting cross-species specificity described herein can be advantageously used in identical form in preclinical testing in non-chimpanzee primates and as drug in humans. These compositions can also be administered in combination with other proteinaceous and non-proteinaceous drugs. These drugs may be administered simultaneously with the composition comprising the bispecific single chain antibody molecule of the invention as defined herein or separately before or after administration of said polypeptide in timely defined intervals and doses. The dosage regimen will be determined by the attending physician and clinical factors. As is well known in the medical arts, dosages for any one patient depend upon many factors, including the patient's size, body surface area, age, the particular compound to be administered, sex, time and route of administration, general health, and other drugs being administered concurrently. Preparations for parenteral administration include sterile aqueous or non-aqueous solutions, suspensions, and emulsions. Examples of non-aqueous solvents are propylene glycol, polyethylene glycol, vegetable oils such as olive oil, and injectable organic esters such as ethyl oleate. Aqueous carriers include water, alcoholic/aqueous solutions, emulsions or suspensions, including saline and buffered media. Parenteral vehicles include sodium chloride solution, Ringer's dextrose, dextrose and sodium chloride, lactated Ringer's, or fixed oils. Intravenous vehicles include fluid and nutrient replenishers, electrolyte replenishers (such as those based on Ringer's dextrose), and the like. Preservatives and other additives may also be present such as, for example, antimicrobials, anti-oxidants, chelating agents, inert gases and the like. In addition, the composition of the present invention might comprise proteinaceous carriers, like, e.g., serum albumin or immunoglobulin, preferably of human origin. It is envisaged that the composition of the invention might comprise, in addition to the bispecific single chain antibody molecule of the invention defined herein, further biologically active agents, depending on the intended use of the composition. Such agents might be drugs acting on the gastro-intestinal system, drugs acting as cytostatica, drugs preventing hyperurikemia, drugs inhibiting immunoreactions (e.g. corticosteroids), drugs modulating the inflammatory response, drugs acting on the circulatory system and/or agents such as cytokines known in the art.

[0143] The biological activity of the pharmaceutical composition defined herein can be determined for instance by cytotoxicity assays, as described in the following examples, in WO 99/54440 or by Schlereth et al. (Cancer Immunol. Immunother. 20 (2005), 1 - 12). "Efficacy" or "in vivo efficacy" as used herein refers to the response to therapy by the pharmaceutical composition of the invention, using e.g. standardized NCI response criteria. The success or *in vivo* efficacy of the therapy using a pharmaceutical composition of the invention refers to the effectiveness of the composition for its intended purpose, i.e. the ability of the composition to cause its desired effect, i.e. depletion of pathologic cells, e.g. tumor cells. The *in vivo* efficacy may be monitored by established standard methods for the respective disease entities including, but not limited to white blood cell counts, differentials, Fluorescence Activated Cell Sorting, bone marrow aspiration. In addition, various disease specific clinical chemistry parameters and other established standard methods may be used. Furthermore, computer-aided tomography, X-ray, nuclear magnetic resonance tomography (e.g. for National Cancer Institute-criteria based response assessment [Cheson BD, Horning SJ, Coiffier B, Shipp MA, Fisher RI, Connors JM, Lister TA, Vose J, Grillo-Lopez A, Hagenbeek A, Cabanillas F, Klippensten D, Hiddemann W, Castellino R, Harris NL, Armitage JO, Carter W, Hoppe R, Canellos GP. Report of an international workshop to standardize response criteria for non-Hodgkin's lymphomas. NCI Sponsored International Working Group. J Clin Oncol. 1999 Apr; 17(4):1244]), positron-emission tomography scanning, white blood cell counts, differentials, Fluorescence Activated Cell Sorting, bone marrow aspiration, lymph node biopsies/histologies, and various cancer specific clinical chemistry parameters (e.g. lactate dehydrogenase) and other established standard methods may be used.

[0144] Another major challenge in the development of drugs such as the pharmaceutical composition of the invention is the predictable modulation of pharmacokinetic properties. To this end, a pharmacokinetic profile of the drug candidate, i.e. a profile of the pharmacokinetic parameters that effect the ability of a particular drug to treat a given condition, is established. Pharmacokinetic parameters of the drug influencing the ability of a drug for treating a certain disease entity include, but are not limited to: half-life, volume of distribution, hepatic first-pass metabolism and the degree of blood serum binding. The efficacy of a given drug agent can be influenced by each of the parameters mentioned above.

[0145] "Half-life" means the time where 50% of an administered drug are eliminated through biological processes, e.g. metabolism, excretion, etc.

[0146] By "hepatic first-pass metabolism" is meant the propensity of a drug to be metabolized upon first contact with the liver, i.e. during its first pass through the liver. "Volume of distribution" means the degree of retention of a drug throughout the various compartments of the body, like e.g. intracellular and extracellular spaces, tissues and organs, etc. and the distribution of the drug within these compartments. "Degree of blood serum binding" means the propensity of a drug to interact with and bind to blood serum proteins, such as albumin, leading to a reduction or loss of biological

activity of the drug.

[0147] Pharmacokinetic parameters also include bioavailability, lag time (Tlag), Tmax, absorption rates, more onset and/or Cmax for a given amount of drug administered. "Bioavailability" means the amount of a drug in the blood compartment.

[0148] "Lag time" means the time delay between the administration of the drug and its detection and measurability in blood or plasma.

[0149] "Tmax" is the time after which maximal blood concentration of the drug is reached, and "Cmax" is the blood concentration maximally obtained with a given drug. The time to reach a blood or tissue concentration of the drug which is required for its biological effect is influenced by all parameters. Pharmacokinetic parameters of bispecific single chain antibodies exhibiting cross-species specificity, which may be determined in preclinical animal testing in non-chimpanzee primates as outlined above are also set forth e.g. in the publication by Schlereth et al. (Cancer Immunol. Immunother. 20 (2005), 1 - 12).

[0150] The term "toxicity" as used herein refers to the toxic effects of a drug manifested in adverse events or severe adverse events. These side events might refer to a lack of tolerability of the drug in general and/or a lack of local tolerance after administration. Toxicity could also include teratogenic or carcinogenic effects caused by the drug.

[0151] The term "safety", "in vivo safety" or "tolerability" as used herein defines the administration of a drug without inducing severe adverse events directly after administration (local tolerance) and during a longer period of application of the drug. "Safety", "in vivo safety" or "tolerability" can be evaluated e.g. at regular intervals during the treatment and follow-up period. Measurements include clinical evaluation, e.g. organ manifestations, and screening of laboratory abnormalities. Clinical evaluation may be carried out and deviating to normal findings recorded/coded according to NCI-CTC and/or MedDRA standards. Organ manifestations may include criteria such as allergy/immunology, blood/bone marrow, cardiac arrhythmia, coagulation and the like, as set forth e.g. in the Common Terminology Criteria for adverse events v3.0 (CTCAE). Laboratory parameters which may be tested include for instance haematology, clinical chemistry, coagulation profile and urine analysis and examination of other body fluids such as serum, plasma, lymphoid or spinal fluid, liquor and the like. Safety can thus be assessed e.g. by physical examination, imaging techniques (i.e. ultrasound, x-ray, CT scans, Magnetic Resonance Imaging (MRI), other measures with technical devices (i.e. electrocardiogram), vital signs, by measuring laboratory parameters and recording adverse events. For example, adverse events in non-chimpanzee primates in the uses and methods according to the invention may be examined by histopathological and/or histochemical methods.

[0152] The term "effective and non-toxic dose" as used herein refers to a tolerable dose of the bispecific single chain antibody as defined herein which is high enough to cause depletion of pathologic cells, tumor elimination, tumor shrinkage or stabilization of disease without or essentially without major toxic effects. Such effective and non-toxic doses may be determined e.g. by dose escalation studies described in the art and should be below the dose inducing severe adverse side events (dose limiting toxicity, DLT).

[0153] The above terms are also referred to e.g. in the Preclinical safety evaluation of biotechnology-derived pharmaceuticals S6; ICH Harmonised Tripartite Guideline; ICH Steering Committee meeting on July 16, 1997.

[0154] Moreover, the invention relates to a pharmaceutical composition comprising a bispecific single chain antibody molecule of this invention or produced according to the process according to the invention for the prevention, treatment or amelioration of cancer. Preferably, said cancer is a solid tumor, preferably a carcinoma or prostate cancer. Preferably, said pharmaceutical composition further comprises suitable formulations of carriers, stabilizers and/or excipients.

[0155] A further aspect of the invention relates to a use of a bispecific single chain antibody molecule/polypeptide as defined herein above or produced according to a process defined herein above, for the preparation of a pharmaceutical composition for the prevention, treatment or amelioration of a disease. Preferably, said disease is cancer. More preferably, said cancer is a solid tumor, preferably a carcinoma or prostate cancer.

[0156] In another preferred embodiment of use of the bispecific single chain antibody molecule of the invention said pharmaceutical composition is suitable to be administered in combination with an additional drug, i.e. as part of a co-therapy. In said co-therapy, an active agent may be optionally included in the same pharmaceutical composition as the bispecific single chain antibody molecule of the invention, or may be included in a separate pharmaceutical composition. In this latter case, said separate pharmaceutical composition is suitable for administration prior to, simultaneously as or following administration of said pharmaceutical composition comprising the bispecific single chain antibody molecule of the invention. The additional drug or pharmaceutical composition may be a non-proteinaceous compound or a proteinaceous compound. In the case that the additional drug is a proteinaceous compound, it is advantageous that the proteinaceous compound be capable of providing an activation signal for immune effector cells.

[0157] Preferably, said proteinaceous compound or non-proteinaceous compound may be administered simultaneously or non-simultaneously with the bispecific single chain antibody molecule of the invention, a nucleic acid molecule as defined hereinabove, a vector as defined hereinabove, or a host as defined hereinabove.

[0158] Another aspect of the invention relates to a method for the prevention, treatment or amelioration of a disease in a subject in the need thereof, said method comprising the step of administration of an effective amount of a pharma-

ceutical composition of the invention. Preferably, said disease is cancer. Preferably, said cancer is a solid tumor, preferably a carcinoma or prostate cancer.

[0159] In another preferred embodiment of the method of the invention said pharmaceutical composition is suitable to be administered in combination with an additional drug, i.e. as part of a co-therapy. In said co-therapy, an active agent may be optionally included in the same pharmaceutical composition as the bispecific single chain antibody molecule of the invention, or may be included in a separate pharmaceutical composition. In this latter case, said separate pharmaceutical composition is suitable for administration prior to, simultaneously as or following administration of said pharmaceutical composition comprising the bispecific single chain antibody molecule of the invention. The additional drug or pharmaceutical composition may be a non-proteinaceous compound or a proteinaceous compound. In the case that the additional drug is a proteinaceous compound, it is advantageous that the proteinaceous compound be capable of providing an activation signal for immune effector cells.

[0160] Preferably, said proteinaceous compound or non-proteinaceous compound may be administered simultaneously or non-simultaneously with the bispecific single chain antibody molecule of the invention, a nucleic acid molecule as defined hereinabove, a vector as defined as defined hereinabove, or a host as defined as defined hereinabove.

[0161] It is preferred for the above described method of the invention that said subject is a human.

[0162] In a further aspect, the invention relates to a kit comprising a bispecific single chain antibody molecule of the invention, a nucleic acid molecule of the invention, a vector of the invention, or a host of the invention.

[0163] These and other embodiments are disclosed and encompassed by the description and Examples of the present invention. Recombinant techniques and methods in immunology are described e.g. in Sambrook et al. Molecular Cloning: A Laboratory Manual; Cold Spring Harbor Laboratory Press, 3rd edition 2001; Lefkovits; Immunology Methods Manual; The Comprehensive Sourcebook of Techniques; Academic Press, 1997; Golemis; Protein-Protein Interactions: A Molecular Cloning Manual; Cold Spring Laboratory Press, 2002. Further literature concerning any one of the antibodies, methods, uses and compounds to be employed in accordance with the present invention may be retrieved from public libraries and databases, using for example electronic devices. For example, the public database "Medline", available on the Internet, may be utilized, for example under <http://www.ncbi.nlm.nih.gov/PubMed/medline.html>. Further databases and addresses such as <http://www.ncbi.nlm.nih.gov/> or listed at the EMBL-services homepage under <http://www.embl.de/services/index.html> are known to the person skilled in the art and can also be obtained using, e. g., <http://www.google.com>.

[0164] The figures show:

Figure 1

Fusion of the N-terminal amino acids 1-27 of primate CD3 epsilon to a heterologous soluble protein.

Figure 2

The figure shows the average absorption values of quadruplicate samples measured in an ELISA assay detecting the presence of a construct consisting of the N-terminal amino acids 1-27 of the mature human CD3 epsilon chain fused to the hinge and Fc gamma portion of human IgG1 and a C-terminal 6 Histidine tag in a supernatant of transiently transfected 293 cells. The first column labeled "27 aa huCD3E" shows the average absorption value for the construct, the second column labeled "irrel. SN" shows the average value for a supernatant of 293 cells transfected with an irrelevant construct as negative control. The comparison of the values obtained for the construct with the values obtained for the negative control clearly demonstrates the presence of the recombinant construct.

Figure 3

The figure shows the average absorption values of quadruplicate samples measured in an ELISA assay detecting the binding of the cross species specific anti-CD3 binding molecules in form of crude preparations of periplasmatically expressed single-chain antibodies to a construct comprising the N-terminal 1-27 amino acids of the mature human CD3 epsilon chain fused to the hinge and Fc gamma portion of human IgG1 and a C-terminal His6 tag. The columns show from left to right the average absorption values for the specificities designated as A2J HLP, I2C HLP E2M HLP, F7O HLP, G4H HLP, H2C HLP, E1L HLP, F12Q HLP, F6A HLP and H1E HLP. The rightmost column labelled "neg. contr." shows the average absorption value for the single-chain preparation of a murine anti-human CD3 antibody as negative control. The comparison of the values obtained for the anti-CD3 specificities with the values obtained for the negative control clearly demonstrates the strong binding of the anti-CD3 specificities to the N-terminal 1-27 amino acids of the mature human CD3 epsilon chain.

Figure 4

Fusion of the N-terminal amino acids 1-27 of primate CD3 epsilon to a heterologous membrane bound protein.

Figure 5

Histogram overlays of different transfectants tested in a FACS assay detecting the presence of recombinant transmembrane fusion proteins consisting of cynomolgus EpCAM and the N-terminal 1-27 amino acids of the human, marmoset, tamarin, squirrel monkey and domestic swine CD3 epsilon chain respectively. The histogram overlays from left to right and top to bottom show the results for the transfectants expressing the constructs comprising the

human 27 mer, marmoset 27 mer, tamarin 27 mer, squirrel monkey 27 mer and swine 27 mer respectively. In the individual overlays the thin line represents a sample incubated with PBS with 2% FCS instead of anti-Flag M2 antibody as negative control and the bold line shows a sample incubated with the anti-Flag M2 antibody. For each construct the overlay of the histograms shows binding of the anti-Flag M2 antibody to the transfectants, which clearly demonstrates the expression of the recombinant constructs on the transfectants.

Figure 6

Histogram overlays of different transfectants tested in a FACS assay detecting the binding of the cross-species specific anti-CD3 binding molecules in form of crude preparations of periplasmatically expressed single-chain antibodies to the N-terminal amino acids 1-27 of the human, marmoset, tamarin and squirrel monkey CD3 epsilon chain respectively fused to cynomolgus EpCAM.

Figure 6A:

The histogram overlays from left to right and top to bottom show the results for the transfectants expressing the 1-27 CD3-EpCAM comprising the human 27 mer tested with the CD3 specific binding molecules designated H2C HLP, F12Q HLP, E2M HLP and G4H HLP respectively.

Figure 6B:

The histogram overlays from left to right and top to bottom show the results for the transfectants expressing the 1-27 CD3-EpCAM comprising the marmoset 27 mer tested with the CD3 specific binding molecules designated H2C HLP, F12Q HLP, E2M HLP and G4H HLP respectively.

Figure 6C:

The histogram overlays from left to right and top to bottom show the results for the transfectants expressing the 1-27 CD3-EpCAM comprising the tamarin 27 mer tested with the CD3 specific binding molecules designated H2C HLP, F12Q HLP, E2M HLP and G4H HLP respectively.

Figure 6D:

The histogram overlays from left to right and top to bottom show the results for the transfectants expressing the 1-27 CD3-EpCAM comprising the squirrel monkey 27 mer tested with the CD3 specific binding molecules designated H2C HLP, F12Q HLP, E2M HLP and G4H HLP respectively.

Figure 6E:

The histogram overlays from left to right and top to bottom show the results for the transfectants expressing the 1-27 CD3-EpCAM comprising the swine 27 mer tested with the CD3 specific binding molecules designated H2C HLP, F12Q HLP, E2M HLP and G4H HLP respectively.

In the individual overlays the thin line represents a sample incubated with a single-chain preparation of a murine anti-human CD3-antibody as negative control and the bold line shows a sample incubated with the respective anti-CD3 binding molecules indicated. Considering the lack of binding to the swine 27 mer transfectants and the expression levels of the constructs shown in Figure 5 the overlays of the histograms show specific and strong binding of the tested anti-CD3 specificities of the fully cross-species specific human bispecific single chain antibodies to cells expressing the recombinant transmembrane fusion proteins comprising the N-terminal amino acids 1-27 of the human, marmoset, tamarin and squirrel monkey CD3 epsilon chain respectively fused to cynomolgus EpCAM and show therefore multi primate cross-species specificity of the anti-CD3 binding molecules.

Figure 7

FACS assay for detection of human CD3 epsilon on transfected murine EL4 T cells. Graphical analysis shows an overlay of histograms. The bold line shows transfected cells incubated with the anti-human CD3 antibody UCHT-1. The thin line represents cells incubated with a mouse IgG1 isotype control. Binding of the anti CD3 antibody UCHT1 clearly shows expression of the human CD3 epsilon chain on the cell surface of transfected murine EL4 T cells.

Figure 8

Binding of cross-species specific anti CD3 antibodies to alanine-mutants in an alanine scanning experiment. In the individual Figures the columns show from left to right the calculated binding values in arbitrary units in logarithmic scale for the wild-type transfectant (WT) and for all alanine-mutants from the position 1 to 27. The binding values are calculated using the following formula:

$$value_Sample(x,y) = \frac{Sample(x,y) - neg_Contr.(x)}{(UCHT-1(x) - neg_Contr.(x)) * \frac{WT(y) - neg_Contr.(wt)}{UCHT-1(wt) - neg_Contr.(wt)}}$$

In this equation *value_Sample* means the value in arbitrary units of binding depicting the degree of binding of a specific anti-CD3 antibody to a specific alanine-mutant as shown in the Figure, *Sample* means the geometric mean fluorescence value obtained for a specific anti-CD3 antibody assayed on a specific alanine-scanning transfectant, *neg_Contr.* means the geometric mean fluorescence value obtained for the negative control assayed on a specific alanine-mutant, *UCHT-1* means the geometric mean fluorescence value obtained for the UCHT-1 antibody assayed on a specific alanine-mutant, *WT* means the geometric mean fluorescence value obtained for a specific anti-CD3 antibody assayed on the wild-type transfectant, *x* specifies the respective transfectant, *y* specifies the respective anti-CD3 antibody and *wt* specifies that the respective transfectant is the wild-type. Individual alanine-mutant positions are labelled with the single letter code of the wild-type amino acid and the number of the position.

Figure 8A:

The figure shows the results for cross-species specific anti CD3 antibody A2J HLP expressed as chimeric IgG molecule. Reduced binding activity is observed for mutations to alanine at position 4 (asparagine), at position 23 (threonine) and at position 25 (isoleucine). Complete loss of binding is observed for mutations to alanine at position 1 (glutamine), at position 2 (aspartate), at position 3 (glycine) and at position 5 (glutamate).

Figure 8B:

The figure shows the results for cross-species specific anti CD3 antibody E2M HLP, expressed as chimeric IgG molecule. Reduced binding activity is observed for mutations to alanine at position 4 (asparagine), at position 23 (threonine) and at position 25 (isoleucine). Complete loss of binding is observed for mutations to alanine at position 1 (glutamine), at position 2 (aspartate), at position 3 (glycine) and at position 5 (glutamate).

Figure 8C:

The figure shows the results for cross-species specific anti CD3 antibody H2C HLP, expressed as chimeric IgG molecule. Reduced binding activity is observed for mutations to alanine at position 4 (asparagine). Complete loss of binding is observed for mutations to alanine glutamine at position 1 (glutamine), at position 2 (aspartate), at position 3 (glycine) and at position 5 (glutamate).

Figure 8D:

shows the results for cross-species specific anti CD3 antibody F12Q HLP, tested as periplasmatically expressed single-chain antibody. Complete loss of binding is observed for mutations to alanine at position 1 (glutamine), at position 2 (aspartate), at position 3 (glycine) and at position 5 (glutamate).

Figure 9

FACS assay detecting the binding of the cross-species specific anti-CD3 binding molecule H2C HLP to human CD3 with and without N-terminal His6 tag.

Histogram overlays are performed of the EL4 cell line transfected with wild-type human CD3 epsilon chain (left histogram) or the human CD3 epsilon chain with N-terminal His6 tag (right histogram) tested in a FACS assay detecting the binding of cross-species specific binding molecule H2C HLP. Samples are incubated with an appropriate isotype control as negative control (thin line), anti-human CD3 antibody UCHT-1 as positive control (dotted line) and cross-species specific anti-CD3 antibody H2C HLP in form of a chimeric IgG molecule (bold line). Histogram overlays show comparable binding of the UCHT-1 antibody to both transfectants as compared to the isotype control demonstrating expression of both recombinant constructs. Histogram overlays also show binding of the anti-CD3 binding molecule H2C HLP only to the wild-type human CD3 epsilon chain but not to the His6-human CD3 epsilon chain. These results demonstrate that a free N-terminus is essential for binding of the cross-species specific anti-CD3 binding molecule H2C HLP.

Figure 10

FACS binding analysis of designated cross-species specific bispecific single chain constructs to CHO cells transfected with the human MCSP D3, human CD3+ T cell line HPB-ALL, CHO cells transfected with cynomolgus MCSP D3 and a macaque T cell line 4119 LnPx. The FACS staining is performed as described in Example 10. The thick line represents cells incubated with 2 µg/ml purified protein that are subsequently incubated with the anti-his antibody and the PE labeled detection antibody. The thin histogram line reflects the negative control: cells only incubated with the anti-his antibody and the detection antibody.

Figure 11

FACS binding analysis of designated cross-species specific bispecific single chain constructs CHO cells transfected with the human MCSP D3, human CD3+ T cell line HPB-ALL, CHO cells transfected with cynomolgus MCSP D3 and a macaque T cell line 4119 LnPx. The FACS staining is performed as described in Example 10. The thick line represents cells incubated with 2 μ g/ml purified protein that are subsequently incubated with the anti-his antibody and the PE labeled detection antibody. The thin histogram line reflects the negative control: cells only incubated with the anti-his antibody and the detection antibody.

Figure 12

FACS binding analysis of designated cross-species specific bispecific single chain constructs CHO cells transfected with the human MCSP D3, human CD3+ T cell line HPB-ALL, CHO cells transfected with cynomolgus MCSP D3 and a macaque T cell line 4119 LnPx. The FACS staining is performed as described in Example 10. The thick line represents cells incubated with 2 μ g/ml purified monomeric protein that are subsequently incubated with the anti-his antibody and the PE labeled detection antibody. The thin histogram line reflects the negative control: cells only incubated with the anti-his antibody and the detection antibody.

Figure 13

Cytotoxicity activity induced by designated cross-species specific MCSP specific single chain constructs redirected to indicated target cell lines. A) Stimulated CD4-/CD56- human PBMCs are used as effector cells, CHO cells transfected with human MCSP D3 as target cells. B) The macaque T cell line 4119 LnPx are used as effector cells, CHO cells transfected with cynomolgus MCSP D3 as target cells. The assay is performed as described in Example 11.

Figure 14

Cytotoxicity activity induced by designated cross-species specific MCSP specific single chain constructs redirected to indicated target cell lines. A) and B) The macaque T cell line 4119 LnPx are used as effector cells, CHO cells transfected with cynomolgus MCSP D3 as target cells. The assay is performed as described in Example 11.

Figure 15

Cytotoxicity activity induced by designated cross-species specific MCSP specific single chain constructs redirected to indicated target cell lines. A) and B) Stimulated CD4-/CD56- human PBMCs are used as effector cells, CHO cells transfected with human MCSP D3 as target cells. The assay is performed as described in Example 11.

Figure 16

Cytotoxicity activity induced by designated cross-species specific MCSP specific single chain constructs redirected to indicated target cell lines. A) Stimulated CD4-/CD56- human PBMCs are used as effector cells, CHO cells transfected with human MCSP D3 as target cells. B) The macaque T cell line 4119 LnPx are used as effector cells, CHO cells transfected with cynomolgus MCSP D3 as target cells. The assay is performed as described in Example 11.

Figure 17

Cytotoxicity activity induced by designated cross-species specific MCSP specific single chain constructs redirected to indicated target cell lines. A) Stimulated CD4-/CD56- human PBMCs are used as effector cells, CHO cells transfected with human MCSP D3 as target cells. B) The macaque T cell line 4119 LnPx are used as effector cells, CHO cells transfected with cynomolgus MCSP D3 as target cells. The assay is performed as described in Example 11.

Figure 18

Plasma stability of MCSP and CD3 cross-species specific bispecific single chain antibodies tested by the measurement of cytotoxicity activity induced by samples of the designated single chain constructs incubated with 50% human plasma at 37°C and 4°C for 24 hours respectively or with addition of 50% human plasma immediately prior to cytotoxicity testing or without addition of plasma. CHO cells transfected with human MCSP are used as target cell line and stimulated CD4-/CD56- human PBMCs are used as effector cells. The assay is performed as described in Example 12.

Figure 19

Initial drop and recovery (i.e. redistribution) of absolute T cell counts (open squares), in peripheral blood of B-NHL patients (patent numbers 1, 7, 23, 30, 31, and 33 of Table 4), who had essentially no circulating CD19-positive target B cells (filled triangles), during the starting phase of intravenous infusion with the CD3 binding molecule CD19xCD3 recognizing a conventional context dependent CD3 epitope. Absolute cell counts are given in 1000 cells per microliter blood. The first data point shows baseline counts immediately prior to the start of infusion. The CD19xCD3 dose is given in parentheses beside the patient number.

Figure 20

(A) Repeated T cell redistribution (open squares) in B-NHL patient #19 (Table 4) who had no circulating CD19-positive target B cells (filled triangles) and developed CNS symptoms under continuous intravenous infusion with CD19xCD3 at a starting dose of 5 μ g/m²/24h for one day followed by a sudden dose increase to 15 μ g/m²/24h. Absolute cell counts are given in 1000 cells per microliter blood. The first data point shows baseline counts immediately prior to the start of infusion. After recovery of circulating T cells from the first episode of redistribution

triggered by the treatment start at $5\mu\text{g}/\text{m}^2/24\text{h}$ the stepwise dose increase from 5 to $15\mu\text{g}/\text{m}^2/24\text{h}$ triggered a second episode of T cell redistribution that was associated with the development of CNS symptoms dominated by confusion and disorientation.

(B) Repeated T cell redistribution in a B-NHL patient, who developed CNS symptoms under repeated intravenous bolus infusion with CD19xCD3 at $1.5\mu\text{g}/\text{m}^2$. Absolute cell counts are given in 1000 cells per microliter blood. The infusion time for each bolus administration was 2 to 4 hours. Vertical arrows indicate the start of bolus infusions. Data points at the beginning of each bolus administration show the T cell counts immediately prior to start of bolus infusion. Each bolus infusion triggered an episode of T cell redistribution followed by recovery of the T cell counts prior to the next bolus infusion. Finally the third episode of T cell redistribution was associated with the development of CNS symptoms in this patient.

Figure 21

Complex T cell redistribution pattern (open squares) in B-NHL patient #20 (Table 4) without circulating CD19-positive target B cells (filled triangles), during ramp initiation of the CD19xCD3 infusion i.e. even gradual increase of flow-rate from almost zero to $15\mu\text{g}/\text{m}^2/24\text{h}$ during the first 24 hours of treatment. Absolute cell counts are given in 1000 cells per microliter blood. The first data point shows baseline counts immediately prior to the start of infusion. The CD19xCD3 dose is given in parentheses beside the patient number. T cells reappearing in the circulating blood after the initial redistribution triggered by the first exposure to CD19xCD3 are partially induced to redisappear from circulating blood again by still increasing levels of CD19xCD3 during the ramp phase.

Figure 22

T and B cell counts during treatment with CD19xCD3 of B-NHL patient #13 (Table 4) who had a significant number of circulating CD19-positive target B (lymphoma) cells (filled triangles). Absolute cell counts are given in 1000 cells per microliter blood. The first data point shows baseline counts immediately prior to the start of infusion. The CD19xCD3 dose is given in parentheses beside the patient number. T cells (open squares) disappear completely from the circulation upon start of CD19xCD3 infusion and do not reappear until the circulating CD19-positive B (lymphoma) cells (filled triangles) are depleted from the peripheral blood.

Figure 23

Repeated T cell redistribution (open squares) in B-NHL patient #24 (Table 4), who had essentially no circulating CD19-positive target B cells (filled triangles) and developed CNS symptoms upon initiation of CD19xCD3 infusion without additional HSA as required for stabilisation of the drug (upper panel). After first recovery of circulating T cells from initial redistribution the uneven drug flow due to the lack of stabilizing HSA triggered a second episode of T cell redistribution that was associated with the development of CNS symptoms dominated by confusion and disorientation. When the same patient was restarted correctly with CD19xCD3 solution containing additional HSA for drug stabilisation, no repeated T cell redistribution was observed (lower panel) and the patient did not again develop any CNS symptoms. Absolute cell counts are given in 1000 cells per microliter blood. The first data point shows baseline counts immediately prior to the start of infusion. The CD19xCD3 dose is given in parentheses beside the patient number.

Figure 24

Model of T cell adhesion to endothelial cells induced by monovalent binding to context dependent CD3 epitopes. Monovalent interaction of a conventional CD3 binding molecule to its context dependent epitope on CD3 epsilon can lead to an allosteric change in the conformation of CD3 followed by the recruitment of Nck2 to the cytoplasmic domain of CD3 epsilon (Gil et al. (2002) Cell 109: 901). As Nck2 is directly linked to integrins via PINCH and ILK (Legate et al. (2006) Nat Rev Mol Cell Biol 7: 20), recruitment of Nck2 to the cytoplasmic domain of CD3 epsilon following an allosteric change in the conformation of CD3 through binding of a conventional CD3 binding molecule (like the CD19xCD3 of example 13) to its context dependent epitope on CD3 epsilon, can increase the adhesiveness of T cells to endothelial cells by transiently switching integrins on the T cell surface into their more adhesive isoform via inside-out-signalling.

Figure 25

Cytotoxic activity of CD33-AF5 VH-VL \times I2C VH-VL test material used for the in vivo study in cynomolgus monkeys as described in Example 14. Specific lysis of CD33-positive target cells was determined in a standard $^{51}\text{Chromium}$ release assay at increasing concentrations of CD33-AF5 VH-VL \times I2C VH-VL. Assay duration was 18 hours. The macaque T cell line 4119 LnPx was used as source of effector cells. CHO cells transfected with cynomolgus CD33 served as target cells. Effector- to target cell ratio (E:T-ratio) was 10:1. The concentration of CD33-AF5 VH-VL \times I2C VH-VL required for half-maximal target cell lysis (EC50) was calculated from the dose response curve with a value of 2.7 ng/ml.

Figure 26

(A) Dose- and time-dependent depletion of CD33-positive monocytes from the peripheral blood of cynomolgus

monkeys through intravenous continuous infusion of CD33-AF5 VH-VL \times I2C VH-VL as described in Example 14. The percentage relative to baseline (i.e. 100%) of absolute circulating CD33-positive monocyte counts after the duration of treatment as indicated above the columns is shown for each of two cynomolgus monkeys per dose level. The dose level (i.e. infusion flow-rate) is indicated below the columns. No depletion of circulating CD33-positive monocytes was observed in animals 1 and 2 treated for 7 days at a dose of 30 $\mu\text{g}/\text{m}^2/24\text{h}$. In animals 3 and 4 treated for 7 days at a dose of 60 $\mu\text{g}/\text{m}^2/24\text{h}$ circulating CD33-positive monocyte counts were reduced to 68% and 40% of baseline, respectively. At 240 $\mu\text{g}/\text{m}^2/24\text{h}$ circulating CD33-positive monocytes were almost completely depleted from the peripheral blood after 3 days of treatment (animals 5 and 6). At 1000 $\mu\text{g}/\text{m}^2/24\text{h}$ depletion of circulating CD33-positive monocytes from the peripheral blood was completed already after 1 day of treatment (animals 7 and 8).

(B) Course of T cell and CD33-monocyte counts in peripheral blood of two cynomolgus monkeys during continuous infusion of CD33-AF5 VH-VL \times I2C VH-VL for 14 days at 120 $\mu\text{g}/\text{m}^2/24\text{h}$. Absolute cell counts are given in 1000 cells per microliter blood. The first data point shows baseline counts immediately prior to the start of infusion. After initial mobilisation of CD33-monocytes during the first 12 hours upon start of infusion CD33-monocytes in peripheral blood (filled triangles) are depleted by two thirds (animal 10) and 50% (animal 9) relative to the respective baseline counts during the further course of infusion. Circulating T cell counts (open squares) show a limited initial drop followed by recovery still during the presence of circulating CD33-positive monocytic target cells.

Figure 27

Cytotoxic activity of MCSP-G4 VH-VL \times I2C VH-VL test material used for the in vivo study in cynomolgus monkeys as described in Example 15. Specific lysis of MCSP-positive target cells was determined in a standard $^{51}\text{Chromium}$ release assay at increasing concentrations of MCSP-G4 VH-VL \times I2C VH-VL. Assay duration was 18 hours. The macaque T cell line 4119 LnPx was used as source of effector cells. CHO cells transfected with cynomolgus MCSP served as target cells. Effector- to target cell ratio (E:T-ratio) was 10:1. The concentration of MCSP-G4 VH-VL \times I2C VH-VL required for half-maximal target cell lysis (EC₅₀) was calculated from the dose response curve with a value of 1.9 ng/ml.

Figure 28

Absence of initial episodes of drop and subsequent recovery of absolute T cell counts (i.e. redistribution) in peripheral blood of cynomolgus monkeys during the starting phase of intravenous infusion with the CD3 binding molecule MCSP-G4 VH-VL \times I2C VH-VL recognizing an essentially context independent CD3 epitope. Absolute cell counts are given in 1000 cells per microliter blood. The first data point shows baseline counts immediately prior to the start of infusion. The MCSP-G4 VH-VL \times I2C VH-VL dose is given in parentheses beside the animal number. In the known absence of MCSP-positive target cells from the circulating blood of cynomolgus monkeys there is no induction of T cell redistribution (i.e. an initial episode of drop and subsequent recovery of absolute T cell counts) through target cell mediated crosslinking of CD3. Moreover, induction of T cell redistribution (i.e. an initial episode of drop and subsequent recovery of absolute T cell counts) through a signal, which the T cells may receive through exclusive interaction with a CD3 binding site only, can be avoided by the use of CD3 binding molecules like MCSP-G4 VH-VL \times I2C VH-VL recognizing an essentially context independent CD3 epitope.

Figure 29

FACS binding analysis of designated cross-species specific bispecific constructs to CHO cells transfected with human CD33, the human CD3+ T cell line HPB-ALL, CHO cells transfected with macaque CD33 and macaque PBMC respectively. The FACS staining is performed as described in Example 16.4. The bold lines represent cells incubated with 5 $\mu\text{g}/\text{ml}$ purified bispecific single chain construct or cell culture supernatant of transfected cells expressing the cross-species specific bispecific antibody constructs. The filled histograms reflect the negative controls. Supernatant of untransfected CHO cells was used as negative control. For each cross-species specific bispecific single chain construct the overlay of the histograms shows specific binding of the construct to human and macaque CD33 and human and macaque CD3.

Figure 30

The diagrams show results of chromium release assays measuring cytotoxic activity induced by designated cross-species specific CD33 specific single chain constructs redirected to the indicated target cell lines. Effector cells were also used as indicated. The assays are performed as described in Example 16.5. The diagrams clearly demonstrate for each construct the potent recruitment of cytotoxic activity of human and macaque effector cells against human and macaque CD33 transfected CHO cells, respectively.

Figure 31

SDS PAGE gel and Western blot monitoring the purification of the cross-species specific bispecific single chain molecule designated E292F3 HL \times I2C HL. Samples from the eluate, the cell culture supernatant (SN) and the flow through of the column (FT) were analyzed as indicated. A protein marker (M) was applied as size reference. A strong

protein band with a molecular weight between 50 and 60 kDa in the SDS PAGE gel demonstrates the efficient purification of the cross-species specific bispecific single chain molecule to a very high degree of purity with the one-step purification method described in Example 17.2. The Western blot detecting the histidines tag confirms the identity of the protein band in the eluate as the cross-species specific bispecific single chain molecule. The faint signal for the flow through sample in this sensitive detection method further shows the nearly complete capture of bispecific single chain molecules by the purification method.

Figure 32

SDS PAGE gel and Western blot monitoring the purification of the cross-species specific bispecific single chain molecule designated V207C12 HL \times H2C HL. Samples from the eluate, the cell culture supernatant (SN) and the flow through of the column (FT) were analyzed as indicated. A protein marker (M) was applied as size reference. A strong protein band with a molecular weight between 50 and 60 kDa in the SDS PAGE gel demonstrates the efficient purification of the cross-species specific bispecific single chain molecule to a very high degree of purity with the one-step purification method described in Example 17.2. The Western blot detecting the histidines tag confirms the identity of the protein band in the eluate as the cross-species specific bispecific single chain molecule. The faint signal for the flow through sample in this sensitive detection method further shows the nearly complete capture of bispecific single chain molecules by the purification method.

Figure 33

SDS PAGE gel and Western blot monitoring the purification of the cross-species specific bispecific single chain molecule designated AF5HLxI2QHL. Samples from the eluate, the cell culture supernatant (SN) and the flow through of the column (FT) were analyzed as indicated. A protein marker (M) was applied as size reference. A strong protein band with a molecular weight between 50 and 60 kDa in the SDS PAGE gel demonstrates the efficient purification of the cross-species specific bispecific single chain molecule to a very high degree of purity with the one-step purification method described in Example 17.2. The Western blot detecting the histidines tag confirms the identity of the protein band in the eluate as the cross-species specific bispecific single chain molecule. The signal in the flow through sample in this sensitive detection method is explained by saturation of the affinity column due to the high concentration of bispecific single chain molecules in the supernatant.

Figure 34

Standard curve of AF5HLxI2CHL in 50% macaque monkey serum. The upper diagram shows the standard curve generated for the assay as described in Example 18.2.

The lower diagram shows results for quality control samples of AF5HLxI2CHL in 50% macaque monkey serum.

The recovery rates are above 90% for the high and mid QC sample and above 80% for the low QC sample.

Thus the assay allows for detection of AF5HLxI2CHL in serum samples in the range from 10 ng/ml to 200 ng/ml (before dilution).

Figure 35

Standard curve of MCSP-G4 HL \times I2C HL in 50% macaque monkey serum. The upper diagram shows the standard curve generated for the assay as described in Example 18.2.

The lower diagram shows results for quality control samples of MCSP-G4 HL \times I2C HL in 50% macaque monkey serum. The recovery rates are above 98% for the high and mid QC sample and above 85% for the low QC sample.

Thus the assay allows for detection of MCSP-G4 HL \times I2C HL in serum samples in the range from 10 ng/ml to 200 ng/ml (before dilution).

Figure 36

FACS binding analysis of an anti-Flag antibody to CHO cells transfected with the 1-27 N-terminal amino acids of CD3 epsilon of the designated species fused to cynomolgus EpCAM. The FACS staining was performed as described in Example 19.1. The bold lines represent cells incubated with the anti-Flag antibody. The filled histograms reflect the negative controls. PBS with 2 % FCS was used as negative control. The histograms show strong and comparable binding of the anti-Flag antibody to all transfectants indicating strong and equal expression of the transfected constructs.

Figure 37

FACS binding analysis of the I2C IgG1 construct to CHO cells expressing the 1-27 N-terminal amino acids of CD3 epsilon of the designated species fused to cynomolgus EpCAM. The FACS staining is performed as described in Example 19.3. The bold lines represent cells incubated with 50 μ l cell culture supernatant of cells expressing the I2C IgG1 construct. The filled histograms reflect the negative control. Cells expressing the 1-27 N-terminal amino acids of CD3 epsilon of swine fused to cynomolgus EpCAM were used as negative control. In comparison with the negative control the histograms clearly demonstrate binding of the I2C IgG1 construct to 1-27 N-terminal amino

acids of CD3 epsilon of human, marmoset, tamarin and squirrel monkey.

Figure 38

FACS binding analysis of the I2C IgG1 construct as described in Example 19.2 to human CD3 with and without N-terminal His6 tag as described in Examples 6.1 and 5.1 respectively. The bold lines represent cells incubated with the anti-human CD3 antibody UCHT-1, the penta-His antibody (Qiagen) and cell culture supernatant of cells expressing the I2C IgG1 construct respectively as indicated. The filled histograms reflect cells incubated with an irrelevant murine IgG1 antibody as negative control.

The upper two histogram overlays show comparable binding of the UCHT-1 antibody to both transfectants as compared to the isotype control demonstrating expression of both recombinant constructs. The centre histogram overlays show binding of the penta his antibody to the cells expressing the His6-human CD3 epsilon chain (His6-CD3) but not to the cells expressing the wild-type CD3 epsilon chain (WT-CD3). The lower Histogram overlays show binding of the I2C IgG1 construct to the wild-type human CD3 epsilon chain but not to the His6-human CD3 epsilon chain. These results demonstrate that a free N-terminus is essential for binding of the cross-species specific anti-CD3 binding molecule I2C to the CD3 epsilon chain.

Figure 39

FACS binding analysis of designated cross-species specific bispecific single chain constructs to CHO cells transfected with human MCSP D3, the human CD3+ T cell line HPB-ALL, CHO cells transfected with macaque MCSP D3 and the macaque T cell line 4119 LnPx respectively. The FACS staining was performed as described in Example 10. The bold lines represents cells incubated with 2 µg/ml purified bispecific single chain construct or cell supernatant containing the bispecific single chain construct respectively. The filled histograms reflect the negative controls. Supernatant of untransfected CHO cells was used as negative control for binding to the T cell lines. A single chain construct with irrelevant target specificity was used as negative control for binding to the MCSP D3 transfected CHO cells. For each cross-species specific bispecific single chain construct the overlay of the histograms shows specific binding of the construct to human and macaque MCSP D3 and human and macaque CD3.

Figure 40

Cytotoxic activity induced by designated cross-species specific MCSP D3 specific single chain constructs redirected to the indicated target cell lines. Effector cells and effector to target ratio were also used as indicated. The assay is performed as described in Example 11. The diagrams clearly demonstrate potent cross-species specific recruitment of cytotoxic activity by each construct.

Figure 41

FACS binding analysis of designated cross-species specific bispecific single chain constructs to CHO cells transfected with human CD33, the human CD3+ T cell line HPB-ALL, CHO cells transfected with macaque CD33 and macaque PBMC respectively. The FACS staining was performed as described in Example 21.2. The bold lines represent cells incubated with cell culture supernatant of transfected cells expressing the cross-species specific bispecific antibody constructs. The filled histograms reflect the negative controls. Supernatant of untransfected CHO cells was used as negative control. For each cross-species specific bispecific single chain construct the overlay of the histograms shows specific binding of the construct to human and macaque CD33 and human and macaque CD3.

Figure 42

The diagrams show results of chromium release assays measuring cytotoxic activity induced by designated cross-species specific CD33 specific single chain constructs redirected to the indicated target cell lines. Effector cells were also used as indicated. The assays are performed as described in Example 21.3. The diagrams clearly demonstrate for each construct the potent recruitment of cytotoxic activity of human and macaque effector cells against human and macaque CD33 transfected CHO cells, respectively.

Figure 43

T cell redistribution in a chimpanzee under weekly intravenous bolus infusion with PBS/5% HSA and PBS/5% HSA plus single-chain EpCAM/CD3-bispecific antibody construct at doses of 1.6, 2.0, 3.0 and 4.5 µg/kg. The infusion time for each bolus administration was 2 hours. Vertical arrows indicate the start of bolus infusions. Data points at the beginning of each bolus administration show the T cell counts immediately prior to start of bolus infusion. Each bolus infusion of the single-chain EpCAM/CD3-bispecific antibody construct, which recognizes a conventional context dependent CD3 epitope, triggered an episode of T cell redistribution followed by recovery of T cells to baseline values prior to the next bolus infusion.

Figure 44

CD3 specific ELISA analysis of periplasmic preparations containing Flag tagged scFv protein fragments from selected clones. Periplasmic preparations of soluble scFv protein fragments were added to wells of an ELISA plate, which had been coated with soluble human CD3 epsilon (aa 1-27)-Fc fusion protein and had been additionally blocked with PBS 3% BSA. Detection was performed by a monoclonal anti Flag-Biotin-labeled antibody followed by perox-

idase-conjugated Streptavidin. The ELISA was developed by an ABTS substrate solution. The OD values (y axis) were measured at 405 nm by an ELISA reader. Clone names are presented on the x axis.

Figure 45

ELISA analysis of periplasmic preparations containing Flag tagged scFv protein fragments from selected clones. The same periplasmic preparations of soluble scFv protein fragments as in Figure 44 were added to wells of an ELISA plate which had not been coated with human CD3 epsilon (aa 1-27)-Fc fusion protein but with hulgG1 (Sigma) and blocked with 3% BSA in PBS.

Detection was performed by a monoclonal anti Flag-Biotin-labeled antibody followed by peroxidase-conjugated Streptavidin. The ELISA was developed by an ABTS substrate solution. The OD values (y axis) were measured at 405 nm by an ELISA reader. Clone names are presented on the x axis.

Figure 46

FACS binding analysis of the designated cross-species specific bispecific single chain constructs to CHO cells transfected with the human PSMA, human CD3+ T cell line HPB-ALL, CHO cells transfected with macaque PSMA and a macaque T cell line 4119 LnPx. The FACS staining is performed as described in Example 24.4. The thick line represents cells incubated with cell culture supernatant that are subsequently incubated with the anti-his antibody and the PE labeled detection antibody. The thin histogram line reflects the negative control: cells only incubated with the anti-his antibody and the detection antibody.

Figure 47

Cytotoxic activity induced by the designated cross-species specific bispecific single chain constructs redirected to indicated target cell lines. A) and B) Stimulated CD4-/CD56- human PBMCs are used as effector cells, CHO cells transfected with human PSMA as target cells. The assay is performed as described in Example 24.5.

Figure 48

Cytotoxic activity induced by the designated cross-species specific bispecific single chain constructs redirected to indicated target cell lines. A) and B) The macaque T cell line 4119 LnPx is used as effector cells, CHO cells transfected with macaque PSMA as target cells. The assay is performed as described in Example 24.5.

Figure 49

FACS binding analysis of the designated cross-species specific bispecific single chain constructs to the human PSMA positive prostate cancer cell line LNCaP, the human CD3+ T cell line HPB-ALL and to the macaque T cell line 4119LnPx respectively. The FACS staining was performed as described in Example 24.7. The bold lines represent cells incubated with cell culture supernatant of transfected cells expressing the cross-species specific bispecific antibody constructs. The filled histograms reflect the negative controls. Cell culture medium was used as a negative control. For each cross-species specific bispecific single chain construct shown the overlay of the histograms demonstrates binding of the construct to human PSMA and human and macaque CD3.

Figure 50

The diagrams show results of chromium release assays measuring cytotoxic activity induced by designated cross-species specific bispecific single chain constructs redirected to the indicated target cell line. Effector cells were also used as indicated. The assays were performed as described in Example 24.8. The diagrams clearly demonstrate for the shown constructs the potent recruitment of cytotoxic activity of human or macaque effector T cells against PSMA-positive cancer cells by the example of the human prostate cancer cell line LNCaP or the macaque cell line 4119LnPx.

Figure 51

FACS binding analysis of the designated cross-species specific bispecific single chain constructs to PSMA positive cells. The FACS staining was performed as described in Example 24.7. For each cross-species specific bispecific single chain construct shown the overlay of the histograms demonstrates binding of the construct to human PSMA and human and macaque CD3.

Figure 52

The diagrams show results of chromium release assays measuring cytotoxic activity induced by designated cross-species specific bispecific single chain constructs redirected to the indicated target cell line. Effector cells were also used as indicated. The assays were performed as described in Example 24.8. The diagrams clearly demonstrate for the shown constructs the potent recruitment of cytotoxic activity of human or macaque effector T cells against PSMA-positive cells.

Figure 53

FACS binding analysis of designated bispecific single chain constructs to CHO cells expressing designated human / rat PSMA chimeras as described in Example 25.1. The FACS staining was performed as described in Example 25.2. The bold lines represent cells incubated with cell culture supernatant of transfected cells expressing the bispecific antibody constructs. The filled histograms show the negative controls. Supernatant of untransfected CHO

cells was used as negative control. For each bispecific single chain construct the overlays of the histograms show specific binding of the construct to the chimeric constructs huPSMArat140-169, huPSMArat191-258, huPSMArat281-284, huPSMArat683-690 and huPSMArat716-750. Compared with the signals obtained for the other bispecific single chain construct there is a clear lack of binding for the bispecific single chain antibody constructs PM84-D7 \times I2C, PM29-G1 \times I2C and PM49-B9 \times I2C to the chimeric construct huPSMArat300-344. Furthermore compared with the signals obtained for the other bispecific single chain constructs there is a clear lack of binding for the bispecific single chain antibody construct PM34-C7 \times I2C to the construct huPSMArat598-617.

Figure 54

Binding of scFv MP9076-A9, the PSMA target binder of PSMA BiTE antibody PM 76-A9 \times I2C to 15-mer peptides spanning over the extracellular domain of human PSMA and overlapping with their neighboring peptides by 14 amino acids. Peptide numbers are plotted on the X-axis. ELISA signals using His detection are plotted on the Y-axis.

Figure 55

Binding of scFv MP9076-B10, the PSMA target binder of PSMA BiTE antibody PM 76-B10 \times I2C to 15-mer peptides spanning over the extracellular domain of human PSMA and overlapping with their neighboring peptides by 14 amino acids. Peptide numbers are plotted on the X-axis. ELISA signals using His detection are plotted on the Y-axis.

Figure 56

Binding of scFv F1-A10, the PSMA target binder of PSMA BiTE antibody PM F1-A10 \times I2C to 15-mer peptides spanning over the extracellular domain of human PSMA and overlapping with their neighboring peptides by 14 amino acids. Peptide numbers are plotted on the X-axis. ELISA signals using His detection are plotted on the Y-axis.

Figure 57

Potential dominant epitopes of scFvs MP 9076-A9, MP 9076-B10 and F1-A10. The potential core binding amino acids in the three-dimensional structure of human PSMA are encircled by a dotted line. Color codes depict scFvs and the respective epitopes. The crystal structure of human PSMA was reported by Davis et al. in 2005 (PNAS, 102: 5981-6).

[0165] The present invention is additionally described by way of the following illustrative non-limiting examples that provide a better understanding of the present invention and of its many advantages.

EXAMPLES

1. Identification of CD3epsilon sequences from blood samples of non-human primates

[0166] Blood samples of the following non-human primates were used for CD3epsilon-identification: *Callithrix jacchus*, *Saguinus oedipus* and *Saimiris ciureus*. Fresh heparin-treated whole blood samples were prepared for isolating total cellular RNA according to manufacturer's protocol (QIAamp RNA Blood Mini Kit, Qiagen). The extracted mRNA was transcribed into cDNA according to published protocols. In brief, 10 μ l of precipitated RNA was incubated with 1.2 μ l of 10x hexanucleotide mix (Roche) at 70 °C for 10 minutes and stored on ice. A reaction mix consisting of 4 μ l of 5x superscript II buffer, 0.2 μ l of 0.1M dithiothreitol, 0.8 μ l of superscript II (Invitrogen), 1.2 μ l of desoxyribonucleoside triphosphates (25 μ M), 0.8 μ l of RNase Inhibitor (Roche) and 1.8 μ l of DNase and RNase free water (Roth) was added. The reaction mix was incubated at room temperature for 10 minutes followed by incubation at 42 °C for 50 minutes and at 90 °C for 5 minutes. The reaction was cooled on ice before adding 0.8 μ l of RNaseH (1 U/ μ l, Roche) and incubated for 20 minutes at 37 °C.

[0167] The first-strand cDNAs from each species were subjected to separate 35-cycle polymerase chain reactions using Taq DNA polymerase (Sigma) and the following primer combination designed on database research: forward primer 5'-AGAGTTCTGGGCCTCTGC-3' (SEQ ID NO: 253); reverse primer 5'-CGGATGGGCTCATAGTCTG-3' (SEQ ID NO: 254). The amplified 550 bp-bands were gel purified (Gel Extraction Kit, Qiagen) and sequenced (Sequisevice, Vaterstetten/Germany, see sequence listing).

CD3epsilon *Callithrix jacchus*

[0168]

Nucleotides

EP 4 180 458 A1

CAGGACGGTAATGAAGAAATGGGTGATACTACACAGAACCCATATAAAGTTTCCATCTCAGG
AACCACAGTAACACTGACATGCCCTCGGTATGATGGACATGAAATAAAATGGCTCGTAAATA
5 GTCAAAACAAAGAAGGTCATGAGGACCACCTGTTACTGGAGGACTTTTCGGAAATGGAGCAA
AGTGGTTATTATGCCTGCCTCTCCAAAGAGACTCCCGCAGAAGAGGCGAGCCATTATCTCTA
CCTGAAGGCAAGAGTGTGTGAGAACTGCGTGGAGGTGGAT

10 Amino acids (SEQ ID NO: 3)

QDGNEEMGDDTTQNPYKVSISGTTVTLTCPRYDGHEIKWLVNSQNKEGHEDHLLLEDFSEMEQ
15 SGYYACLSKETPAEEASHYLYLKARVCENCVEVD

CD3epsilon *Saguinus oedipus*

[0169]

20 Nucleotides

CAGGACGGTAATGAAGAAATGGGTGATACTACACAGAACCCATATAAAGTTTCCATCTCAGG
AACCACAGTAACACTGACATGCCCTCGGTATGATGGACATGAAATAAAATGGCTTGTAATA
25 GTCAAAACAAAGAAGGTCATGAGGACCACCTGTTACTGGAGGATTTTTCGGAAATGGAGCAA
AGTGGTTATTATGCCTGCCTCTCCAAAGAGACTCCCGCAGAAGAGGCGAGCCATTATCTCTA
CCTGAAGGCAAGAGTGTGTGAGAACTGCGTGGAGGTGGAT

30 Amino acids (SEQ ID NO: 5)

QDGNEEMGDDTTQNPYKVSISGTTVTLTCPRYDGHEIKWLVNSQNKEGHEDHLLLEDFSEMEQ
35 SGYYACLSKETPAEEASHYLYLKARVCENCVEVD

CD3epsilon *Saimiris ciureus*

[0170]

40 Nucleotides

CAGGACGGTAATGAAGAGATTGGTGATACTACCCAGAACCCATATAAAGTTTCCATCTCAGG
45 AACCACAGTAACACTGACATGCCCTCGGTATGATGGACAGGAAATAAAATGGCTCGTAAATG
ATCAAAACAAAGAAGGTCATGAGGACCACCTGTTACTGGAAGATTTTTCAGAAATGGAACAA
AGTGGTTATTATGCCTGCCTCTCCAAAGAGACCCCCACAGAAGAGGCGAGCCATTATCTCTA
50 CCTGAAGGCAAGAGTGTGTGAGAACTGCGTGGAGGTGGAT

Amino acids (SEQ ID NO: 7)

QDGNEEIGDDTTQNPYKVSISGTTVTLTCPRYDGQEIKWLVNDQNKEGHEDHLLLEDFSEMEQ
55 SGYYACLSKETPTEEASHYLYLKARVCENCVEVD

2. Generation of cross-species specific single chain antibody fragments (scFv) binding to the N-terminal amino acids 1-27 of CD3epsilon of man and different non-chimpanzee primates

2.1. Immunization of mice using the N-terminus of CD3epsilon separated from its native CD3-context by fusion to a heterologous soluble protein

[0171] Ten weeks old F1 mice from balb/c × C57black crossings were immunized with the CD3epsilon-Fc fusion protein carrying the most N-terminal amino acids 1-27 of the mature CD3epsilon chain (1-27 CD3-Fc) of man and/or saimiris ciureus. To this end 40 µg of the 1-27 CD3-Fc fusion protein with 10 nmol of a thioate-modified CpG-Oligonucleotide (5'-tccatgacgttcctgatgct-3') (SEQ ID No. 343) in 300 µl PBS were injected per mouse intra-peritoneally. Mice receive booster immunizations after 21, 42 and optionally 63 days in the same way. Ten days after the first booster immunization, blood samples were taken and antibody serum titer against 1-27 CD3-Fc fusion protein was tested by ELISA. Additionally, the titer against the CD3-positive human T cell line HPBALL was tested in flow cytometry according to standard protocols. Serum titers were significantly higher in immunized than in non-immunized animals.

2.2. Generation of an immune murine antibody scFv library: Construction of a combinatorial antibody library and phage display

[0172] Three days after the last injection the murine spleen cells were harvested for the preparation of total RNA according to standard protocols.

[0173] A library of murine immunoglobulin (Ig) light chain (kappa) variable region (VK) and Ig heavy chain variable region (VH) DNA-fragments was constructed by RT-PCR on murine spleen RNA using VK- and VH specific primer. cDNA was synthesized according to standard protocols.

[0174] The primers were designed in a way to give rise to a 5'-XhoI and a 3'-BstEII recognition site for the amplified heavy chain V-fragments and to a 5'-SacI and a 3'-SpeI recognition site for amplified VK DNA fragments.

[0175] For the PCR-amplification of the VH DNA-fragments eight different 5'-VH-family specific primers (MVH1(GC)AG GTG CAG CTC GAG GAG TCA GGA CCT (SEQ ID No. 344); MVH2 GAG GTC CAG CTC GAG CAG TCT GGA CCT (SEQ ID No. 345); MVH3 CAG GTC CAA CTC GAG CAG CCT GGG GCT (SEQ ID No. 346); MVH4 GAG GTT CAG CTC GAG CAG TCT GGG GCA (SEQ ID No. 347); MVH5 GA(AG) GTG AAG CTC GAG GAG TCT GGA GGA (SEQ ID No. 348); MVH6 GAG GTG AAG CTT CTC GAG TCT GGA GGT (SEQ ID No. 349); MVH7 GAA GTG AAG CTC GAG GAG TCT GGG GGA (SEQ ID No. 350); MVH8 GAG GTT CAG CTC GAG CAG TCT GGA GCT (SEQ ID No. 351)) were each combined with one 3'-VH primer (3'MuVHBstEII tga gga gac ggt gac cgt ggt ccc ttg gcc cca g (SEQ ID No. 352)); for the PCR amplification of the VK-chain fragments seven different 5'-VK-family specific primers (MUVK1 CCA GTT CCG AGC TCG TTG TGA CTC AGG AAT CT (SEQ ID No. 353); MUVK2 CCA GTT CCG AGC TCG TGT TGA CGC AGC CGC CC (SEQ ID No. 354); MUVK3 CCA GTT CCG AGC TCG TGC TCA CCC AGT CTC CA (SEQ ID No. 355); MUVK4 CCA GTT CCG AGC TCC AGA TGA CCC AGT CTC CA (SEQ ID No. 356); MUVK5 CCA GAT GTG AGC TCG TGA TGA CCC AGA CTC CA (SEQ ID No. 357); MUVK6 CCA GAT GTG AGC TCG TCA TGA CCC AGT CTC CA (SEQ ID No. 358); MUVK7 CCA GTT CCG AGC TCG TGA TGA CAC AGT CTC CA (SEQ ID No. 359)) were each combined with one 3'-VK primer (3'MuVkHindIII/BsiW1 tgg tgc act agt cgt acg ttg gat etc aag ctt ggt ccc (SEQ ID No. 360)).

[0176] The following PCR program was used for amplification: denaturation at 94°C for 20 sec; primer annealing at 52°C for 50 sec and primer extension at 72°C for 60 sec and 40 cycles, followed by a 10 min final extension at 72°C.

[0177] 450 ng of the kappa light chain fragments (SacI-SpeI digested) were ligated with 1400 ng of the phagemid pComb3H5BHis (SacI-SpeI digested; large fragment). The resulting combinatorial antibody library was then transformed into 300 µl of electrocompetent Escherichia coli XL1 Blue cells by electroporation (2.5 kV, 0.2 cm gap cuvette, 25 µFD, 200 Ohm, Biorad gene-pulser) resulting in a library size of more than 10⁷ independent clones. After one hour of phenotype expression, positive transformants were selected for carbenicillin resistance encoded by the pComb3H5BHis vector in 100 ml of liquid super broth (SB)-culture overnight. Cells were then harvested by centrifugation and plasmid preparation was carried out using a commercially available plasmid preparation kit (Qiagen).

[0178] 2800 ng of this plasmid-DNA containing the VK-library (XhoI-BstEII digested; large fragment) were ligated with 900 ng of the heavy chain V-fragments (XhoI-BstEII digested) and again transformed into two 300 µl aliquots of electrocompetent E. coli XL1 Blue cells by electroporation (2.5 kV, 0.2 cm gap cuvette, 25 µFD, 200 Ohm) resulting in a total VH-VK scFv (single chain variable fragment) library size of more than 10⁷ independent clones.

[0179] After phenotype expression and slow adaptation to carbenicillin, the E. coli cells containing the antibody library were transferred into SB-Carbenicillin (50 µg/mL) selection medium. The E. coli cells containing the antibody library were then infected with an infectious dose of 10¹² particles of helper phage VCSM13 resulting in the production and secretion of filamentous M13 phage, wherein phage particle contains single stranded pComb3H5BHis-DNA encoding a murine scFv-fragment and displayed the corresponding scFv-protein as a translational fusion to phage coat protein

III. This pool of phages displaying the antibody library was later used for the selection of antigen binding entities.

2.3. Phage display based selection of CD3-specific binders

[0180] The phage library carrying the cloned scFv-repertoire was harvested from the respective culture supernatant by PEG8000/NaCl precipitation and centrifugation. Approximately 10^{11} to 10^{12} scFv phage particles were resuspended in 0.4 ml of PBS/0.1% BSA and incubated with 10^5 to 10^7 Jurkat cells (a CD3-positive human T-cell line) for 1 hour on ice under slow agitation. These Jurkat cells were grown beforehand in RPMI medium enriched with fetal calf serum (10 %), glutamine and penicillin/streptomycin, harvested by centrifugation, washed in PBS and resuspended in PBS/1 % FCS (containing Na Azide). scFv phage which do not specifically bind to the Jurkat cells were eliminated by up to five washing steps with PBS/1 % FCS (containing Na Azide). After washing, binding entities were eluted from the cells by resuspending the cells in HCl-glycine pH 2.2 (10 min incubation with subsequent vortexing) and after neutralization with 2 M Tris pH 12, the eluate was used for infection of a fresh uninfected E. coli XL1 Blue culture (OD600 > 0.5). The E. coli culture containing E. coli cells successfully transduced with a phagemid copy, encoding a human scFv-fragment, were again selected for carbenicillin resistance and subsequently infected with VCMS 13 helper phage to start the second round of antibody display and in vitro selection. A total of 4 to 5 rounds of selections were carried out, normally.

2.4. Screening for CD3-specific binders

[0181] Plasmid DNA corresponding to 4 and 5 rounds of panning was isolated from E. coli cultures after selection. For the production of soluble scFv-protein, VH-VL-DNA fragments were excised from the plasmids (XhoI-SpeI). These fragments were cloned via the same restriction sites in the plasmid pComb3H5BFlag/His differing from the original pComb3H5BHis in that the expression construct (e.g. scFv) includes a Flag-tag (TGD YKDDDDK) between the scFv and the His6-tag and the additional phage proteins were deleted. After ligation, each pool (different rounds of panning) of plasmid DNA was transformed into 100 μ l heat shock competent E. coli TG1 or XLI blue and plated onto carbenicillin LB-agar. Single colonies were picked into 100 μ l of LB carb (50 μ g/ml).

[0182] E. coli transformed with pComb3H5BHis containing a VL- and VH-segment produce soluble scFv in sufficient amounts after excision of the gene III fragment and induction with 1 mM IPTG. Due to a suitable signal sequence, the scFv-chain was exported into the periplasma where it folds into a functional conformation.

[0183] Single E. coli TG1 bacterial colonies from the transformation plates were picked for periplasmic small scale preparations and grown in SB-medium (e.g. 10 ml) supplemented with 20 mM MgCl₂ and carbenicillin 50 μ g/ml (and re-dissolved in PBS (e.g. 1 ml) after harvesting. By four rounds of freezing at -70°C and thawing at 37°C, the outer membrane of the bacteria was destroyed by temperature shock and the soluble periplasmic proteins including the scFvs were released into the supernatant. After elimination of intact cells and cell-debris by centrifugation, the supernatant containing the human anti-human CD3-scFvs was collected and used for further examination.

2.5. Identification of CD3-specific binders

[0184] Binding of the isolated scFvs was tested by flow cytometry on eukaryotic cells, which on their surface express a heterologous protein displaying at its N-terminus the first 27 N-terminal amino acids of CD3epsilon.

[0185] As described in Example 4, the first amino acids 1-27 of the N-terminal sequence of the mature CD3 epsilon chain of the human T cell receptor complex (amino acid sequence: QDGNEEMGGITQTPYKVSISGTTVILT SEQ ID NO: 2) were fused to the N-terminus of the transmembrane protein EpCAM so that the N-terminus was located at the outer cell surface. Additionally, a FLAG epitope was inserted between the N-terminal 1-27 CD3epsilon sequence and the EpCAM sequence. This fusion product was expressed in human embryonic kidney (HEK) and chinese hamster ovary (CHO) cells.

[0186] Eukaryotic cells displaying the 27 most N-terminal amino acids of mature CD3epsilon of other primate species were prepared in the same way for Saimiri ciureus (Squirrel monkey) (CD3epsilon N-terminal amino acid sequence: QDGNEEIGDTTQNPYKVSISGTTVTLT SEQ ID NO: 8), for Callithrix jacchus (CD3epsilon N-terminal amino acid sequence: QDGNEEMGDTTQNPYKVSISGTTVTLT SEQ ID NO: 4) and for Saguinus oedipus (CD3epsilon N-terminal amino acid sequence: QDGNEEMGDTTQNPYKVSISGTTVTLT SEQ ID NO: 6).

[0187] For flow cytometry 2.5×10^5 cells are incubated with 50 μ l supernatant or with 5 μ g/ml of the purified constructs in 50 μ l PBS with 2% FCS. The binding of the constructs was detected with an anti-His antibody (Penta-His Antibody, BSA free, Qiagen GmbH, Hilden, FRG) at 2 μ g/ml in 50 μ l PBS with 2% FCS. As a second step reagent a R-Phycoerythrin-conjugated affinity purified F(ab')₂ fragment, goat anti-mouse IgG (Fc-gamma fragment specific), diluted 1:100 in 50 μ l PBS with 2% FCS (Dianova, Hamburg, FRG) was used. The samples were measured on a FACSScan (BD biosciences, Heidelberg, FRG).

[0188] Binding was always confirmed by flowcytometry as described in the foregoing paragraph on primary T cells of

man and different primates (e.g. saimiris ciureus, callithrix jacchus, saguinus oedipus).

2.6. Generation of human/humanized equivalents of non-human CD3epsilon specific scFvs

[0189] The VH region of the murine anti-CD3 scFv was aligned against human antibody germline amino acid sequences. The human antibody germline VH sequence was chosen which has the closest homology to the non-human VH and a direct alignment of the two amino acid sequences was performed. There were a number of framework residues of the non-human VH that differ from the human VH framework regions ("different framework positions"). Some of these residues may contribute to the binding and activity of the antibody to its target.

[0190] To construct a library that contain the murine CDRs and at every framework position that differs from the chosen human VH sequence both possibilities (the human and the maternal murine amino acid residue), degenerated oligonucleotides were synthesized. These oligonucleotides incorporate at the differing positions the human residue with a probability of 75 % and the murine residue with a probability of 25 %. For one human VH e.g. six of these oligonucleotides had to be synthesized that overlap in a terminal stretch of approximately 20 nucleotides. To this end every second primer was an antisense primer. Restriction sites needed for later cloning within the oligonucleotides were deleted.

[0191] These primers may have a length of 60 to 90 nucleotides, depending on the number of primers that were needed to span over the whole V sequence.

[0192] These e.g. six primers were mixed in equal amounts (e.g. 1 µl of each primer (primer stocks 20 to 100 µM) to a 20 µl PCR reaction) and added to a PCR mix consisting of PCR buffer, nucleotides and Taq polymerase. This mix was incubated at 94 °C for 3 minutes, 65 °C for 1 minute, 62°C for 1 minute, 59 °C for 1 minute, 56 °C for 1 minute, 52 °C for 1 minute, 50 °C for 1 minute and at 72°C for 10 minutes in a PCR cycler. Subsequently the product was run in an agarose gel electrophoresis and the product of a size from 200 to 400 isolated from the gel according to standard methods.

[0193] This PCR product was then used as a template for a standard PCR reaction using primers that incorporate N-terminal and C-terminal suitable cloning restriction sites. The DNA fragment of the correct size (for a VH approximately 350 nucleotides) was isolated by agarose gel electrophoresis according to standard methods. In this way sufficient VH DNA fragment was amplified. This VH fragment was now a pool of VH fragments that have each one a different amount of human and murine residues at the respective differing framework positions (pool of humanized VH). The same procedure was performed for the VL region of the murine anti-CD3 scFv (pool of humanized VL).

[0194] The pool of humanized VH was then combined with the pool of humanized VL in the phage display vector pComb3H5Bhis to form a library of functional scFvs from which - after display on filamentous phage - anti-CD3 binders were selected, screened, identified and confirmed as described above for the parental non-human (murine) anti-CD3 scFv. Single clones were then analyzed for favorable properties and amino acid sequence. Those scFvs which were closest in amino acid sequence homology to human germline V-segments are preferred particularly those wherein at least one CDR among CDR I and II of VH and CDR I and II of VLkappa or CDR I and II of VLlambda shows more than 80% amino acid sequence identity to the closest respective CDR of all human germline V-segments. Anti-CD3 scFvs were converted into recombinant bispecific single chain antibodies as described in the following Examples 9, 16, and 24.

3. Generation of a recombinant fusion protein of the N-terminal amino acids 1-27 of the human CD3 epsilon chain fused to the Fc-part of an IgG1 (1-27 CD3-Fc).

3.1. Cloning and expression of 1-27 CD3-Fc

[0195] The coding sequence of the 1-27 N-terminal amino acids of the human CD3 epsilon chain fused to the hinge and Fc gamma region of human immunoglobulin IgG1 as well as an 6 Histidine Tag were obtained by gene synthesis according to standard protocols (cDNA sequence and amino acid sequence of the recombinant fusion protein are listed under SEQ ID NOs 230 and 229). The gene synthesis fragment was designed as to contain first a Kozak site for eukaryotic expression of the construct, followed by an 19 amino acid immunoglobulin leader peptide, followed in frame by the coding sequence of the first 27 amino acids of the extracellular portion of the mature human CD3 epsilon chain, followed in frame by the coding sequence of the hinge region and Fc gamma portion of human IgG1, followed in frame by the coding sequence of a 6 Histidine tag and a stop codon (Figure 1). The gene synthesis fragment was also designed as to introduce restriction sites at the beginning and at the end of the cDNA coding for the fusion protein. The introduced restriction sites, EcoRI at the 5' end and Sall at the 3' end, are utilized in the following cloning procedures. The gene synthesis fragment was cloned via EcoRI and Sall into a plasmid designated pEF-DHFR (pEF-DHFR is described in Mack et al. Proc. Natl. Acad. Sci. USA 92 (1995) 7021-7025 and Raum et al. Cancer Immunol Immunother 50 (2001) 141-150) following standard protocols. A sequence verified plasmid was used for transfection in the FreeStyle 293 Expression System (Invitrogen GmbH, Karlsruhe, Germany) according to the manufacturers protocol. After 3 days cell culture supernatants of the transfectants were harvested and tested for the presence of the recombinant construct in

an ELISA assay. Goat anti-human IgG, Fc-gamma fragment specific antibody (obtained from Jackson ImmunoResearch Europe Ltd., Newmarket, Suffolk, UK) was diluted in PBS to 5 µg/ml and coated with 100 µl per well onto a MaxiSorp 96-well ELISA plate (Nunc GmbH & Co. KG, Wiesbaden, Germany) over night at 4 °C. Wells were washed with PBS with 0,05 % Tween 20 (PBS/Tween and blocked with 3 % BSA in PBS (bovine Albumin, fraction V, Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany) for 60 minutes at room temperature (RT). Subsequently, wells were washed again PBS/Tween and then incubated with cell culture supernatants for 60 minutes at RT. After washing wells were incubated with a peroxidase conjugated anti-His6 antibody (Roche Diagnostics GmbH, Roche Applied Science, Mannheim, Germany) diluted 1:500 in PBS with 1 % BSA for 60 minutes at RT. Subsequently, wells were washed with 200 µl PBS/Tween and 100 µl of the SIGMAFAST OPD (SIGMAFAST OPD [o-Phenylenediamine dihydrochloride] substrate solution (Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany) was added according to the manufacturers protocol. The reaction was stopped by adding 100 µl 1 M H₂SO₄. Color reaction was measured on a PowerWaveX microplate spectrophotometer (BioTek Instruments, Inc., Winooski, Vermont, USA) at 490 nm and subtraction of background absorption at 620 nm. As shown in Figure 2 presence of the construct as compared to irrelevant supernatant of mock-transfected HEK 293 cells used as negative control was clearly detectable.

3.2. Binding assay of cross-species specific single chain antibodies to 1-27 CD3-Fc.

[0196] Binding of crude preparations of periplasmatically expressed cross-species specific single chain antibodies specific for CD3 epsilon to 1-27 CD3-Fc was tested in an ELISA assay. Goat anti-human IgG, Fc-gamma fragment specific antibody (Jackson ImmunoResearch Europe Ltd., Newmarket, Suffolk, UK) was diluted in PBS to 5 µg/ml and coated with 100 µl per well onto a MaxiSorp 96-well ELISA plate (Nunc GmbH & Co. KG, Wiesbaden, Germany) over night at 4 °C. Wells were washed with PBS with 0,05 % Tween 20 (PBS/Tween and blocked with PBS with 3 % BSA (bovine Albumin, fraction V, Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany) for 60 minutes at RT. Subsequently, wells were washed with PBS/Tween and incubated with supernatants of cells expressing the 1-27 CD3-Fc construct for 60 minutes at RT. Wells were washed with PBS/Tween and incubated with crude preparations of periplasmatically expressed cross-species specific single-chain antibodies as described above for 60 minutes at room temperature. After washing with PBS/Tween wells were incubated with peroxidase conjugated anti-Flag M2 antibody (Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany) diluted 1 :10000 in PBS with 1 % BSA for 60 minutes at RT. Wells were washed with PBS/Tween and incubated with 100 µl of the SIGMAFAST OPD (OPD [o-Phenylenediamine dihydrochloride] substrate solution (Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany) according to the manufacturers protocol. Color reaction was stopped with 100 µl 1 M H₂SO₄ and measured on a PowerWaveX microplate spectrophotometer (BioTek Instruments, Inc., Winooski, Vermont, USA) at 490 nm and subtraction of background absorption at 620 nm. Strong binding of cross-species specific human single chain antibodies specific for CD3 epsilon to the 1-27 CD3-Fc construct compared to a murine anti CD3 single-chain antibody was observed (Figure 3).

4. Generation of recombinant transmembrane fusion proteins of the N-terminal amino acids 1-27 of CD3 epsilon from different non-chimpanzee primates fused to EpCAM from cynomolgus monkey (1-27 CD3-EpCAM).

4.1. Cloning and expression of 1-27 CD3-EpCAM

[0197] CD3 epsilon was isolated from different non-chimpanzee primates (marmoset, tamarin, squirrel monkey) and swine. The coding sequences of the 1-27 N-terminal amino acids of CD3 epsilon chain of the mature human, common marmoset (*Callithrix jacchus*), cottontop tamarin (*Saguinus oedipus*), common squirrel monkey (*Saimiri sciureus*) and domestic swine (*Sus scrofa*; used as negative control) fused to the N-terminus of Flag tagged cynomolgus EpCAM were obtained by gene synthesis according to standard protocols. cDNA sequence and amino acid sequence of the recombinant fusion proteins are listed under SEQ ID NOs 231 to 240). The gene synthesis fragments were designed as to contain first a BsrGI site to allow fusion in correct reading frame with the coding sequence of a 19 amino acid immunoglobulin leader peptide already present in the target expression vector, which is followed in frame by the coding sequence of the N-terminal 1-27 amino acids of the extracellular portion of the mature CD3 epsilon chains, which is followed in frame by the coding sequence of a Flag tag and followed in frame by the coding sequence of the mature cynomolgus EpCAM transmembrane protein (Figure 4). The gene synthesis fragments were also designed to introduce a restriction site at the end of the cDNA coding for the fusion protein. The introduced restriction sites BsrGI at the 5' end and Sall at the 3' end, were utilized in the following cloning procedures. The gene synthesis fragments were then cloned via BsrGI and Sall into a derivative of the plasmid designated pEF DHFR (pEF-DHFR is described in Mack et al. Proc. Natl. Acad. Sci. USA 92 (1995) 7021-7025), which already contained the coding sequence of the 19 amino acid immunoglobulin leader peptide following standard protocols. Sequence verified plasmids were used to transiently transfect 293-HEK cells using the MATra-A Reagent (IBA GmbH, Göttingen, Germany) and 12 µg of plasmid DNA for adherent 293-HEK cells in 175 ml cell culture flasks according to the manufacturers protocol. After 3 days of cell culture the

transfectants were tested for cell surface expression of the recombinant transmembrane protein via an FACS assay according to standard protocols. For that purpose a number of $2,5 \times 10^5$ cells were incubated with the anti-Flag M2 antibody (Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany) at 5 µg/ml in PBS with 2% FCS. Bound antibody was detected with an R-Phycoerythrin-conjugated affinity purified F(ab')₂ fragment, goat anti-mouse IgG, Fc-gamma fragment specific 1:100 in PBS with 2% FCS (Jackson ImmunoResearch Europe Ltd., Newmarket, Suffolk, UK). The samples were measured on a FACScalibur (BD biosciences, Heidelberg, Germany). Expression of the Flag tagged recombinant transmembrane fusion proteins consisting of cynomolgus EpCAM and the 1-27 N-terminal amino acids of the human, marmoset, tamarin, squirrel monkey and swine CD3 epsilon chain respectively on transfected cells was clearly detectable (Figure 5).

4.2. Binding of cross-species specific anti-CD3 single chain antibodies to the 1-27 CD3-EpCAM

[0198] Binding of crude preparations of periplasmatically expressed cross-species specific anti CD3 single-chain antibodies to the 1-27 N-terminal amino acids of the human, marmoset, tamarin and squirrel monkey CD3 epsilon chains respectively fused to cynomolgus Ep-CAM was tested in an FACS assay according to standard protocols. For that purpose a number of $2,5 \times 10^5$ cells were incubated with crude preparations of periplasmatically expressed cross-species specific anti CD3 single-chain antibodies (preparation was performed as described above and according to standard protocols) and a single-chain murine anti-human CD3 antibody as negative control. As secondary antibody the Penta-His antibody (Qiagen GmbH, Hildesheim, Germany) was used at 5 µg/ml in 50 µl PBS with 2% FCS. The binding of the antibody was detected with an R-Phycoerythrin-conjugated affinity purified F(ab')₂ fragment, goat anti-mouse IgG, Fc-gamma fragment specific, diluted 1:100 in PBS with 2% FCS (Jackson ImmunoResearch Europe Ltd., Newmarket, Suffolk, UK). The samples were measured on a FACScalibur (BD biosciences, Heidelberg, Germany). As shown in Figures 6 (A to E) binding of single chain antibodies to the transfectants expressing the recombinant transmembrane fusion proteins consisting of the 1-27 N-terminal amino acids of CD3 epsilon of the human, marmoset, tamarin or squirrel monkey fused to cynomolgus EpCAM was observed. No binding of cross-species specific single chain antibodies was observed to a fusion protein consisting of the 1-27 N-terminal CD3 epsilon of swine fused to cynomolgus EpCAM used as negative control. Multi-primate cross-species specificity of the anti-CD3 single chain antibodies was shown. Signals obtained with the anti Flag M2 antibody and the cross-species specific single chain antibodies were comparable, indicating a strong binding activity of the cross-species specific single chain antibodies to the N-terminal amino acids 1-27 of CD3 epsilon.

5. Binding analysis of cross-species specific anti-CD3 single chain antibodies by alanine-scanning of mouse cells transfected with the human CD3 epsilon chain and its alanine mutants

5.1. Cloning and expression of human wild-type CD3 epsilon

[0199] The coding sequence of the human CD3 epsilon chain was obtained by gene synthesis according to standard protocols (cDNA sequence and amino acid sequence of the human CD3 epsilon chain are listed under SEQ ID NOs 242 and 241). The gene synthesis fragment was designed as to contain a Kozak site for eukaryotic expression of the construct and restriction sites at the beginning and the end of the cDNA coding for human CD3 epsilon. The introduced restriction sites EcoRI at the 5' end and Sall at the 3' end, were utilized in the following cloning procedures. The gene synthesis fragment was then cloned via EcoRI and Sall into a plasmid designated pEF NEO following standard protocols. pEF NEO was derived of pEF DHFR (Mack et al. Proc. Natl. Acad. Sci. USA 92 (1995) 7021-7025) by replacing the cDNA of the DHFR with the cDNA of the neomycin resistance by conventional molecular cloning. A sequence verified plasmid was used to transfect the murine T cell line EL4 (ATCC No. TIB-39) cultivated in RPMI with stabilized L-glutamine supplemented with 10 % FCS, 1% penicillin/streptomycin, 1% HEPES, 1% pyruvate, 1% non-essential amino acids (all Biochrom AG Berlin, Germany) at 37 °C, 95 % humidity and 7 % CO₂. Transfection was performed with the SuperFect Transfection Reagent (Qiagen GmbH, Hilden, Germany) and 2 µg of plasmid DNA according to the manufacturer's protocol. After 24 hours the cells were washed with PBS and cultivated again in the aforementioned cell culture medium with 600 µg/ml G418 for selection (PAA Laboratories GmbH, Pasching, Austria). 16 to 20 days after transfection the outgrowth of resistant cells was observed. After additional 7 to 14 days cells were tested for expression of human CD3 epsilon by FACS analysis according to standard protocols. $2,5 \times 10^5$ cells were incubated with anti-human CD3 antibody UCHT-1 (BD biosciences, Heidelberg, Germany) at 5 µg/ml in PBS with 2% FCS. The binding of the antibody was detected with an R-Phycoerythrin-conjugated affinity purified F(ab')₂ fragment, goat anti-mouse IgG, Fc-gamma fragment specific, diluted 1:100 in PBS with 2% FCS (Jackson ImmunoResearch Europe Ltd., Newmarket, Suffolk, UK). The samples were measured on a FACScalibur (BD biosciences, Heidelberg, Germany). Expression of human wild-type CD3 on transfected EL4 cells is shown in Figure 7.

5.2. Cloning and expression of the cross-species specific anti-CD3 single chain antibodies as IgG1 antibodies

[0200] In order to provide improved means of detection of binding of the cross-species specific single chain anti-CD3 antibodies H2C HLP, A2J HLP and E2M HLP were converted into IgG1 antibodies with murine IgG1 and human lambda constant regions. cDNA sequences coding for the heavy and light chains of respective IgG antibodies were obtained by gene synthesis according to standard protocols. The gene synthesis fragments for each specificity were designed as to contain first a Kozak site to allow eukaryotic expression of the construct, which is followed by an 19 amino acid immunoglobulin leader peptide (SEQ ID NOs 244 and 243), which is followed in frame by the coding sequence of the respective heavy chain variable region or respective light chain variable region, followed in frame by the coding sequence of the heavy chain constant region of murine IgG1 (SEQ ID NOs 246 and 245) or the coding sequence of the human lambda light chain constant region (SEQ ID NO 248 and 247), respectively. Restriction sites were introduced at the beginning and the end of the cDNA coding for the fusion protein. Restriction sites EcoRI at the 5' end and Sall at the 3' end were used for the following cloning procedures. The gene synthesis fragments were cloned via EcoRI and Sall into a plasmid designated pEF DHFR (Mack et al. Proc. Natl. Acad. Sci. USA 92 (1995) 7021-7025) for the heavy chain constructs and pEF ADA (pEF ADA is described in Raum et al., Cancer Immunol Immunother., 50(3), (2001), 141-50) for the light chain constructs) according to standard protocols. Sequence verified plasmids were used for co-transfection of respective light and heavy chain constructs in the FreeStyle 293 Expression System (Invitrogen GmbH, Karlsruhe, Germany) according to the manufacturers protocol. After 3 days cell culture supernatants of the transfectants were harvested and used for the alanine-scanning experiment.

5.3. Cloning and expression of alanine mutants of human CD3 epsilon for alanine-scanning

[0201] 27 cDNA fragments coding for the human CD3 epsilon chain with an exchange of one codon of the wild-type sequence of human CD3 epsilon into a codon coding for alanine (GCC) for each amino acid of amino acids 1-27 of the extracellular domain of the mature human CD3 epsilon chain respectively were obtained by gene synthesis. Except for the exchanged codon the cDNA fragments were identical to the aforementioned human wild-type CD3 cDNA fragment. Only one codon was replaced in each construct compared to the human wild-type CD3 cDNA fragment described above. Restriction sites EcoRI and Sall were introduced into the cDNA fragments at identical positions compared to the wild-type construct. All alanine-scanning constructs were cloned into pEF NEO and sequence verified plasmids were transfected into EL4 cells. Transfection and selection of transfectants was performed as described above. As result a panel of expressed constructs was obtained wherein the first amino acid of the human CD3 epsilon chain, glutamine (Q, Gln) at position 1 was replaced by alanine. The last amino acid replaced by alanine was the threonine (T, Thr) at position 27 of mature human wild-type CD3 epsilon. For each amino acid between glutamine 1 and threonine 27 respective transfectants with an exchange of the wild-type amino acid into alanine were generated.

5.4. Alanine-scanning experiment

[0202] Chimeric IgG antibodies as described in 5.2 and cross-species specific single chain antibodies specific for CD3 epsilon were tested in alanine-scanning experiment. Binding of the antibodies to the EL4 cell lines transfected with the alanine-mutant constructs of human CD3 epsilon as described in 5.3 was tested by FACS assay according to standard protocols. 2.5×10^5 cells of the respective transfectants were incubated with 50 μ l of cell culture supernatant containing the chimeric IgG antibodies or with 50 μ l of crude preparations of periplasmatically expressed single-chain antibodies. For samples incubated with crude preparations of periplasmatically expressed single-chain antibodies the anti-Flag M2 antibody (Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany) was used as secondary antibody at 5 μ g/ml in 50 μ l PBS with 2% FCS. For samples incubated with the chimeric IgG antibodies a secondary antibody was not necessary. For all samples the binding of the antibody molecules was detected with an R-Phycoerythrin-conjugated affinity purified F(ab')₂ fragment, goat anti-mouse IgG, Fc-gamma fragment specific, diluted 1:100 in PBS with 2% FCS (Jackson ImmunoResearch Europe Ltd., Newmarket, Suffolk, UK). Samples were measured on a FACSCalibur (BD biosciences, Heidelberg, Germany). Differential binding of chimeric IgG molecules or cross-species specific single-chain antibodies to the EL4 cell lines transfected with the alanine-mutants of human CD3 epsilon was detected. As negative control either an isotype control or a crude preparation of a periplasmatically expressed single-chain antibody of irrelevant specificity was used respectively. UCHT-1 antibody was used as positive control for the expression level of the alanine-mutants of human CD3 epsilon. The EL4 cell lines transfected with the alanine-mutants for the amino acids tyrosine at position 15, valine at position 17, isoleucine at position 19, valine at position 24 or leucine at position 26 of the mature CD3 epsilon chain were not evaluated due to very low expression levels (data not shown). Binding of the cross-species specific single chain antibodies and the single chain antibodies in chimeric IgG format to the EL4 cell lines transfected with the alanine-mutants of human CD3 epsilon is shown in Figure 8 (A-D) as relative binding in arbitrary units with the geometric mean fluorescence values of the respective negative controls subtracted from all respective geometric mean

fluorescence sample values. To compensate for different expression levels all sample values for a certain transfectant were then divided through the geometric mean fluorescence value of the UCHT-1 antibody for the respective transfectant. For comparison with the wild-type sample value of a specificity all sample values of the respective specificity were finally divided through the wild-type sample value, thereby setting the wild-type sample value to 1 arbitrary unit of binding.

[0203] The calculations used are shown in detail in the following formula:

$$value_Sample(x, y) = \frac{Sample(x, y) - neg_Contr.(x)}{(UCHT-1(x) - neg_Contr.(x)) * \frac{WT(y) - neg_Contr.(wt)}{UCHT-1(wt) - neg_Contr.(wt)}}$$

[0204] In this equation *value_Sample* means the value in arbitrary units of binding depicting the degree of binding of a specific anti-CD3 antibody to a specific alanine-mutant as shown in Figure 8 (A-D), *Sample* means the geometric mean fluorescence value obtained for a specific anti-CD3 antibody assayed on a specific alanine-scanning transfectant, *neg_Contr.* means the geometric mean fluorescence value obtained for the negative control assayed on a specific alanine-mutant, *UCHT-1* means the geometric mean fluorescence value obtained for the UCHT-1 antibody assayed on a specific alanine-mutant, *WT* means the geometric mean fluorescence value obtained for a specific anti-CD3 antibody assayed on the wild-type transfectant, *x* specifies the respective transfectant, *y* specifies the respective anti-CD3 antibody and *wt* specifies that the respective transfectant is the wild-type.

[0205] As can be seen in Figure 8 (A-D) the IgG antibody A2J HLP showed a pronounced loss of binding for the amino acids asparagine at position 4, threonine at position 23 and isoleucine at position 25 of the mature CD3 epsilon chain. A complete loss of binding of IgG antibody A2J HLP was observed for the amino acids glutamine at position 1, aspartate at position 2, glycine at position 3 and glutamate at position 5 of the mature CD3 epsilon chain. IgG antibody E2M HLP showed a pronounced loss of binding for the amino acids asparagine at position 4, threonine at position 23 and isoleucine at position 25 of the mature CD3 epsilon chain. IgG antibody E2M HLP showed a complete loss of binding for the amino acids glutamine at position 1, aspartate at position 2, glycine at position 3 and glutamate at position 5 of the mature CD3 epsilon chain. IgG antibody H2C HLP showed an intermediate loss of binding for the amino acid asparagine at position 4 of the mature CD3 epsilon chain and it showed a complete loss of binding for the amino acids glutamine at position 1, aspartate at position 2, glycine at position 3 and glutamate at position 5 of the mature CD3 epsilon chain. Single chain antibody F12Q HLP showed an essentially complete loss of binding for the amino acids glutamine at position 1, aspartate at position 2, glycine at position 3 of the mature CD3 epsilon chain and glutamate at position 5 of the mature CD3 epsilon chain.

6. Binding analysis of the cross-species specific anti-CD3 binding molecule H2C HLP to the human CD3 epsilon chain with and without N-terminal His6 tag transfected into the murine T cell line EL4

6.1. Cloning and expression of the human CD3 epsilon chain with N-terminal six histidine tag (His6 tag)

[0206] A cDNA fragment coding for the human CD3 epsilon chain with a N-terminal His6 tag was obtained by gene synthesis. The gene synthesis fragment was designed as to contain first a Kozak site for eukaryotic expression of the construct, which is followed in frame by the coding sequence of a 19 amino acid immunoglobulin leader peptide, which is followed in frame by the coding sequence of a His6 tag which is followed in frame by the coding sequence of the mature human CD3 epsilon chain (the cDNA and amino acid sequences of the construct are listed as SEQ ID NOs 256 and 255). The gene synthesis fragment was also designed as to contain restriction sites at the beginning and the end of the cDNA. The introduced restriction sites EcoRI at the 5' end and Sall at the 3' end, were used in the following cloning procedures. The gene synthesis fragment was then cloned via EcoRI and Sall into a plasmid designated pEF-NEO (as described above) following standard protocols. A sequence verified plasmid was used to transfect the murine T cell line EL4. Transfection and selection of the transfectants were performed as described above. After 34 days of cell culture the transfectants were used for the assay described below.

6.2. Binding of the cross-species specific anti-CD3 binding molecule H2C HLP to the human CD3 epsilon chain with and without N-terminal His6 tag

[0207] A chimeric IgG antibody with the binding specificity H2C HLP specific for CD3 epsilon was tested for binding to human CD3 epsilon with and without N-terminal His6 tag. Binding of the antibody to the EL4 cell lines transfected the His6-human CD3 epsilon and wild-type human CD3 epsilon respectively was tested by an FACS assay according to standard protocols. 2.5×10^5 cells of the transfectants were incubated with 50 μ l of cell culture supernatant containing

the chimeric IgG antibody or 50 μ l of the respective control antibodies at 5 μ g/ml in PBS with 2% FCS. As negative control an appropriate isotype control and as positive control for expression of the constructs the CD3 specific antibody UCHT-1 were used respectively. The binding of the antibodies was detected with a R-Phycoerythrin-conjugated affinity purified F(ab')₂ fragment, goat anti-mouse IgG, Fc-gamma fragment specific, diluted 1:100 in PBS with 2% FCS (Jackson ImmunoResearch Europe Ltd., Newmarket, Suffolk, UK). Samples were measured on a FACSCalibur (BD biosciences, Heidelberg, Germany). Compared to the EL4 cell line transfected with wild-type human CD3 epsilon a clear loss of binding of the chimeric IgG with binding specificity H2C HLP to human-CD3 epsilon with an N-terminal His6 tag was detected. These results showed that a free N-terminus of CD3 epsilon is essential for binding of the cross-species specific anti-CD3 binding specificity H2C HLP to the human CD3 epsilon chain (Figure 9).

7. Cloning and expression of the C-terminal, transmembrane and truncated extracellular domains of human MCSP

[0208] The coding sequence of the C-terminal, transmembrane and truncated extracellular domain of human MCSP (amino acids 1538 - 2322) was obtained by gene synthesis according to standard protocols (cDNA sequence and amino acid sequence of the recombinant construct for expression of the C-terminal, transmembrane and truncated extracellular domain of human MCSP (designated as human D3) are listed under SEQ ID NOs 250 and 249). The gene synthesis fragment was designed as to contain first a Kozak site to allow eukaryotic expression of the construct followed by the coding sequence of an 19 amino acid immunoglobulin leader peptide followed in frame by a FLAG tag, followed in frame by a sequence containing several restriction sites for cloning purposes and coding for a 9 amino acid artificial linker (SRTRSGSQL), followed in frame by the coding sequence of the C-terminal, transmembrane and truncated extracellular domain of human MCSP and a stop codon. Restriction sites were introduced at the beginning and at the end of the DNA fragment. The restriction sites EcoRI at the 5' end and Sall at the 3' end were used in the following cloning procedures. The fragment was digested with EcoRI and Sall and cloned into pEF-DHFR (pEF-DHFR is described in Mack et al. Proc. Natl. Acad. Sci. USA 92 (1995) 7021-7025) following standard protocols. A sequence verified plasmid was used to transfect CHO/dhfr- cells (ATCC No. CRL 9096). Cells were cultivated in RPMI 1640 with stabilized glutamine, supplemented with 10% FCS, 1% penicillin/streptomycin (all obtained from Biochrom AG Berlin, Germany) and nucleosides from a stock solution of cell culture grade reagents (Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany) to a final concentration of 10 μ g/ml Adenosine, 10 μ g/ml Deoxyadenosine and 10 μ g/ml Thymidine, in an incubator at 37 °C, 95% humidity and 7% CO₂. Transfection was performed using the PolyFect Transfection Reagent (Qiagen GmbH, Hilden, Germany) and 5 μ g of plasmid DNA according to the manufacturer's protocol. After cultivation for 24 hours cells were washed once with PBS and cultivated again in RPMI 1640 with stabilized glutamine and 1% penicillin/streptomycin. Thus the cell culture medium did not contain nucleosides and thereby selection was applied on the transfected cells. Approximately 14 days after transfection the outgrowth of resistant cells was observed. After an additional 7 to 14 days the transfectants were tested for expression of the construct by FACS analysis. $2,5 \times 10^5$ cells were incubated with 50 μ l of an anti-Flag-M2 antibody (Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany) diluted to 5 μ g/ml in PBS with 2% FCS. The binding of the antibody was detected with a R-Phycoerythrin-conjugated affinity purified F(ab')₂ fragment, goat anti-mouse IgG, Fc-gamma fragment specific diluted 1:100 in PBS with 2% FCS (ImmunoResearch Europe Ltd., Newmarket, Suffolk, UK). The samples were measured on a FACSCalibur (BD biosciences, Heidelberg, Germany).

8. Cloning and expression of the C-terminal, transmembrane and truncated extracellular domains of macaque MCSP

[0209] The cDNA sequence of the C-terminal, transmembrane and truncated extracellular domains of macaque MCSP (designated as macaque D3) was obtained by a set of three PCRs on macaque skin cDNA (Cat No. C1534218-Cy-BC; BioCat GmbH, Heidelberg, Germany) using the following reaction conditions: 1 cycle at 94°C, 3 min., 40 cycles with 94°C for 0,5 min., 52°C for 0,5 min. and 72°C for 1,75 min., terminal cycle of 72°C for 3 min.. The following primers were used:

forward primer: 5'-GATCTGGTCTACACCATCGAGC-3' (SEQ ID No. 361)
reverse primer: 5'-GGAGCTGCTGCTGGCTCAGTGAGG-3' (SEQ ID No. 362)
forward primer: 5'- TTCCAGCTGAGCATGTCTGATGG-3' (SEQ ID No. 363)
reverse primer: 5'- CGATCAGCATCTGGGCCAGG-3' (SEQ ID No. 364)
forward primer: 5'- GTGGAGCAGTTCACTCAGCAGGACC-3' (SEQ ID No. 365)
reverse primer: 5'- GCCTTCACACCCAGTACTGGCC-3' (SEQ ID No. 366)

[0210] Those PCRs generated three overlapping fragments (A: 1-1329, B: 1229-2428, C: 1782-2547) which were isolated and sequenced according to standard protocols using the PCR primers and thereby provided a 2547 bp portion of the cDNA sequence of macaque MCSP (the cDNA sequence and amino acid sequence of this portion of macaque

MCSP are listed under SEQ ID NOs 252 and 251) from 74 bp upstream of the coding sequence of the C-terminal domain to 121 bp downstream of the stop codon. Another PCR using the following reaction conditions: 1 cycle at 94°C for 3 min, 10 cycles with 94°C for 1 min, 52°C for 1 min and 72°C for 2,5 min, terminal cycle of 72°C for 3 min was used to fuse the PCR products of the aforementioned reactions A and B. The following primers are used:

forward primer: 5'-tcccgtacgagatctggatcccaattggatggcggactcgtgctgttctcacacagagg-3' (SEQ ID No. 367)
reverse primer: 5'-agtgggtcgactcacaccagactaggccattcttaagggcaggg-3' (SEQ ID No. 368)

[0211] The primers for this PCR were designed to introduce restriction sites at the beginning and at the end of the cDNA fragment coding for the C-terminal, transmembrane and truncated extracellular domains of macaque MCSP. The introduced restriction sites MfeI at the 5' end and Sall at the 3' end, were used in the following cloning procedures. The PCR fragment was then cloned via MfeI and Sall into a Bluescript plasmid containing the EcoRI/MfeI fragment of the aforementioned plasmid pEF-DHFR (pEF-DHFR is described in Raum et al. Cancer Immunol Immunother 50 (2001) 141-150) by replacing the C-terminal, transmembrane and truncated extracellular domains of human MCSP. The gene synthesis fragment contained the coding sequences of the immunoglobulin leader peptide and the Flag tag as well as the artificial linker (SRTRSGSQL) in frame to the 5' end of the cDNA fragment coding for the C-terminal, transmembrane and truncated extracellular domains of macaque MCSP. This vector was used to transfect CHO/dhfr- cells (ATCC No. CRL 9096). Cells were cultivated in RPMI 1640 with stabilized glutamine supplemented with 10% FCS, 1% penicillin/streptomycin (all from Biochrom AG Berlin, Germany) and nucleosides from a stock solution of cell culture grade reagents (Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany) to a final concentration of 10 µg/ml Adenosine, 10 µg/ml Deoxyadenosine and 10 µg/ml Thymidine, in an incubator at 37 °C, 95% humidity and 7% CO₂. Transfection was performed with PolyFect Transfection Reagent (Qiagen GmbH, Hilden, Germany) and 5 µg of plasmid DNA according to the manufacturer's protocol. After cultivation for 24 hours cells were washed once with PBS and cultivated again in RPMI 1640 with stabilized glutamine and 1% penicillin/streptomycin. Thus the cell culture medium did not contain nucleosides and thereby selection was applied on the transfected cells. Approximately 14 days after transfection the outgrowth of resistant cells is observed. After an additional 7 to 14 days the transfectants were tested for expression of the recombinant construct via FACS. 2,5×10⁵ cells were incubated with 50 µl of an anti-Flag-M2 antibody (Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany) diluted to 5 µg/ml in PBS with 2% FCS. Bound antibody was detected with a R-Phycoerythrin-conjugated affinity purified F(ab')₂ fragment, goat anti-mouse IgG, Fc-gamma fragment specific, diluted 1:100 in PBS with 2% FCS (Jackson ImmunoResearch Europe Ltd., Newmarket, Suffolk, UK). Samples were measured on a FACScalibur (BD biosciences, Heidelberg, Germany).

9. Generation and characterisation of MCSP and CD3 cross-species specific bispecific single chain molecules

[0212] Bispecific single chain antibody molecules each comprising a binding domain cross-species specific for human and non-chimpanzee primate CD3 epsilon as well as a binding domain cross-species-specific for human and non-chimpanzee primate MCSP, are designed as set out in the following Table 1:

Table 1: Formats of MCSP and CD3 cross-species specific bispecific single chain antibodies

SEQ ID (nucl/prot)	Formats of protein constructs (N → C)
190/189	MCSP-G4 HL × H2C HL
192/191	MCSP-G4 HL × F12Q HL
194/193	MCSP-G4 HL × I2C HL
196/195	MCSP-G4 HLP × F6A HLP
198/197	MCSP-G4 HLP × H2C HLP
202/201	MCSP-G4 HLP × G4H HLP
206/205	MCSP-G4 HLP × E1L HLP
208/207	MCSP-G4 HLP × E2M HLP
212/211	MCSP-G4 HLP × F12Q HL
214/213	MCSP-G4 HLP × I2C HL
216/215	MCSP-D2 HL × H2C HL
218/217	MCSP-D2 HL × F12Q HL

(continued)

SEQ ID (nucl/prot)	Formats of protein constructs (N → C)
220/219	MCSP-D2 HL × I2C HL
222/221	MCSP-D2 HLP × H2C HLP
224/223	MCSP-F9 HL × H2C HL
226/225	MCSP-F9 HLP × H2C HLP
228/227	MCSP-F9 HLP × G4H HLP
318/317	MCSP-A9 HL × H2C HL
320/319	MCSP-A9 HL × F12Q HL
322/321	MCSP-A9 HL × I2C HL
324/323	MCSP-C8 HL × I2C HL
328/327	MCSP-B7 HL × I2C HL
326/325	MCSP-B8 HL × I2C HL
330/329	MCSP-G8 HL × I2C HL
332/331	MCSP-D5 HL × I2C HL
334/333	MCSP-F7 HL × I2C HL
336/335	MCSP-G5 HL × I2C HL
338/337	MCSP-F8 HL × I2C HL
340/339	MCSP-G10 HL × I2C HL

[0213] The aforementioned constructs containing the variable heavy-chain (VH) and variable light-chain (VL) domains cross-species specific for human and macaque MCSP D3 and the VH and VL domains cross-species specific for human and macaque CD3 were obtained by gene synthesis. The gene synthesis fragments were designed as to contain first a Kozak site for eukaryotic expression of the construct, followed by a 19 amino acid immunoglobulin leader peptide, followed in frame by the coding sequence of the respective bispecific single chain antibody molecule, followed in frame by the coding sequence of a histidine₆-tag and a stop codon. The gene synthesis fragment was also designed as to introduce suitable N- and C-terminal restriction sites. The gene synthesis fragment was cloned via these restriction sites into a plasmid designated pEF-DHFR (pEF-DHFR is described in Raum et al. Cancer Immunol Immunother 50 (2001) 141-150) according to standard protocols (Sambrook, Molecular Cloning; A Laboratory Manual, 3rd edition, Cold Spring Harbour Laboratory Press, Cold Spring Harbour, New York (2001)). The constructs were transfected stably or transiently into DHFR-deficient CHO-cells (ATCC No. CRL 9096) by electroporation or alternatively into HEK 293 (human embryonal kidney cells, ATCC Number: CRL-1573) in a transient manner according to standard protocols.

[0214] Eukaryotic protein expression in DHFR deficient CHO cells (ATCC No. CRL 9096) was performed as described by Kaufmann R.J. (1990) Methods Enzymol. 185, 537-566. Gene amplification of the constructs was induced by addition of increasing concentrations of methothrexate (MTX) up to final concentrations of 20 nM MTX. After two passages of stationary culture the cells were grown in roller bottles with nucleoside-free HyQ PF CHO liquid soy medium (with 4.0 mM L-Glutamine with 0.1% Pluronic F - 68; HyClone) for 7 days before harvest. The cells were removed by centrifugation and the supernatant containing the expressed protein is stored at - 20°C.

[0215] Äkta® Explorer System (GE Health Systems) and Unicorn® Software were used for chromatography. Immobilized metal affinity chromatography ("IMAC") was performed using a Fractogel EMD chelate® (Merck) which was loaded with ZnCl₂ according to the protocol provided by the manufacturer. The column was equilibrated with buffer A (20 mM sodium phosphate buffer pH 7.2, 0.1 M NaCl) and the cell culture supernatant (500 ml) was applied to the column (10 ml) at a flow rate of 3 ml/min. The column was washed with buffer A to remove unbound sample. Bound protein was eluted using a two step gradient of buffer B (20 mM sodium phosphate buffer pH 7.2, 0.1 M NaCl, 0.5 M Imidazole) according to the following:

- Step 1: 20% buffer B in 6 column volumes
Step 2: 100% buffer B in 6 column volumes

[0216] Eluted protein fractions from step 2 were pooled for further purification. All chemicals are of research grade and purchased from Sigma (Deisenhofen) or Merck (Darmstadt).

[0217] Gel filtration chromatography was performed on a HiLoad 16/60 Superdex 200 prep grade column (GE/Amer-sham) equilibrated with Equi-buffer (25 mM Citrate, 200 mM Lysine, 5% Glycerol, pH 7.2). Eluted protein samples (flow rate 1 ml/min) were subjected to standard SDS-PAGE and Western Blot for detection. Prior to purification, the column was calibrated for molecular weight determination (molecular weight marker kit, Sigma MW GF-200). Protein concentrations were determined using OD280 nm.

[0218] Purified bispecific single chain antibody protein was analyzed in SDS PAGE under reducing conditions performed with pre-cast 4-12% Bis Tris gels (Invitrogen). Sample preparation and application were performed according to the protocol provided by the manufacturer. The molecular weight was determined with MultiMark protein standard (Invitrogen). The gel was stained with colloidal Coomassie (Invitrogen protocol). The purity of the isolated protein is >95% as determined by SDS-PAGE.

[0219] The bispecific single chain antibody has a molecular weight of about 52 kDa under native conditions as determined by gel filtration in phosphate buffered saline (PBS). All constructs were purified according to this method.

[0220] Western Blot was performed using an Optitran® BA-S83 membrane and the Invitrogen Blot Module according to the protocol provided by the manufacturer. For detection of the bispecific single chain antibody protein antibodies an anti-His Tag antibody was used (Penta His, Qiagen). A Goat-anti-mouse Ig antibody labeled with alkaline phosphatase (AP) (Sigma) was used as secondary antibody and BCIP/NBT (Sigma) as substrate. A single band was detected at 52 kD corresponding to the purified bispecific single chain antibody.

[0221] Alternatively, constructs were transiently expressed in DHFR deficient CHO cells. In brief, 4×10^5 cells per construct were cultivated in 3 ml RPMI 1640 all medium with stabilized glutamine supplemented with 10% fetal calf serum, 1% penicillin/streptomycin and nucleosides from a stock solution of cell culture grade reagents (Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany) to a final concentration of 10 µg/ml Adenosine, 10 µg/ml Deoxyadenosine and 10 µg/ml Thymidine, in an incubator at 37 °C, 95% humidity and 7% CO₂ one day before transfection. Transfection was performed with Fugene 6 Transfection Reagent (Roche, # 11815091001) according to the manufacturer's protocol. 94 µl OptiMEM medium (Invitrogen) and 6 µl Fugene 6 are mixed and incubated for 5 minutes at room temperature. Subsequently, 1.5 µg DNA per construct were added, mixed and incubated for 15 minutes at room temperature. Meanwhile, the DHFR deficient CHO cells were washed with 1x PBS and resuspended in 1.5 ml RPMI 1640 all medium. The transfection mix was diluted with 600 µl RPMI 1640 all medium, added to the cells and incubated overnight at 37 °C, 95% humidity and 7% CO₂. The day after transfection the incubation volume of each approach was extended to 5 ml RPMI 1640 all medium. Supernatant was harvested after 3 days of incubation.

10. Flow cytometric binding analysis of the MCSP and CD3 cross-species specific bispecific antibodies

[0222] In order to test the functionality of the cross-species specific bispecific antibody constructs regarding the capability to bind to human and macaque MCSP D3 and CD3, respectively, a FACS analysis was performed. For this purpose CHO cells transfected with human MCSP D3 (as described in Example 7) and the human CD3 positive T cell leukemia cell line HPB-ALL (DSMZ, Braunschweig, ACC483) were used to test the binding to human antigens. The binding reactivity to macaque antigens was tested by using the generated macaque MCSP D3 transfectant (described in Example 8) and a macaque T cell line 4119LnPx (kindly provided by Prof. Fickenscher, Hygiene Institute, Virology, Erlangen-Nuernberg; published in Knappe A, et al., and Fickenscher H., Blood 2000, 95, 3256-61). 200.000 cells of the respective cell lines were incubated for 30 min on ice with 50 µl of the purified protein of the cross-species specific bispecific antibody constructs (2 µg/ml) or cell culture supernatant of transfected cells expressing the cross-species specific bispecific antibody constructs. The cells were washed twice in PBS with 2% FCS and binding of the construct was detected with a murine anti-His antibody (Penta His antibody; Qiagen; diluted 1:20 in 50 µl PBS with 2% FCS). After washing, bound anti-His antibodies were detected with an Fc gamma-specific antibody (Dianova) conjugated to phycoerythrin, diluted 1:100 in PBS with 2% FCS. Supernatant of untransfected CHO cells was used as negative control for binding to the T cell lines. A single chain construct with irrelevant target specificity was used as negative control for binding to the MCSP-D3 transfected CHO cells.

[0223] Flow cytometry was performed on a FACS-Calibur apparatus; the CellQuest software was used to acquire and analyze the data (Becton Dickinson biosciences, Heidelberg). FACS staining and measuring of the fluorescence intensity were performed as described in Current Protocols in Immunology (Coligan, Kruisbeek, Margulies, Shevach and Strober, Wiley-Interscience, 2002).

[0224] The bispecific binding of the single chain molecules listed above, which are cross-species specific for MCSP D3 and cross-species specific for human and macaque CD3 was clearly detectable as shown in Figures 10, 11, 12 and 39. In the FACS analysis all constructs showed binding to CD3 and MCSP D3 as compared to the respective negative controls. Cross-species specificity of the bispecific antibodies to human and macaque CD3 and MCSP D3 antigens was demonstrated.

11. Bioactivity of MCSP and CD3 cross-species specific bispecific single chain antibodies

[0225] Bioactivity of the generated bispecific single chain antibodies was analyzed by chromium 51 (⁵¹Cr) release in vitro cytotoxicity assays using the MCSP D3 positive cell lines described in Examples 7 and 8. As effector cells stimulated human CD4/CD56 depleted PBMC, stimulated human PBMC or the macaque T cell line 4119LnPx are used as specified in the respective figures.

[0226] Generation of the stimulated CD4/CD56 depleted PBMC was performed as follows:

Coating of a Petri dish (145 mm diameter, Greiner bio-one GmbH, Kremsmünster) was carried out with a commercially available anti-CD3 specific antibody (e.g. OKT3, Othoclone) in a final concentration of 1 µg/ml for 1 hour at 37°C. Unbound protein was removed by one washing step with PBS. The fresh PBMC were isolated from peripheral blood (30 - 50 ml human blood) by Ficoll gradient centrifugation according to standard protocols. $3 - 5 \times 10^7$ PBMC were added to the precoated petri dish in 120 ml of RPMI 1640 with stabilized glutamine /10% FCS / IL-2 20 U/ml (Proleukin, Chiron) and stimulated for 2 days. On the third day the cells were collected and washed once with RPMI 1640. IL-2 was added to a final concentration of 20 U/ml and the cells were cultivated again for one day in the same cell culture medium as above. By depletion of CD4+ T cells and CD56+ NK cells according to standard protocols CD8+ cytotoxic T lymphocytes (CTLs) were enriched.

[0227] Target cells were washed twice with PBS and labelled with 11.1 MBq ⁵¹Cr in a final volume of 100 µl RPMI with 50% FCS for 45 minutes at 37°C. Subsequently the labelled target cells were washed 3 times with 5 ml RPMI and then used in the cytotoxicity assay. The assay was performed in a 96 well plate in a total volume of 250 µl supplemented RPMI (as above) with an E:T ratio 10:1. 1 µg/ml of the cross-species specific bispecific single chain antibody molecules and 20 threefold dilutions thereof were applied. If using supernatant containing the cross-species specific bispecific single chain antibody molecules, 21 two- and 20 threefold dilutions thereof were applied for the macaque and the human cytotoxicity assay, respectively. The assay time was 18 hours and cytotoxicity was measured as relative values of released chromium in the supernatant related to the difference of maximum lysis (addition of Triton-X) and spontaneous lysis (without effector cells). All measurements were done in quadruplicates. Measurement of chromium activity in the supernatants was performed with a Wizard 3" gamma counter (Perkin Elmer Life Sciences GmbH, Köln, Germany). Analysis of the experimental data was performed with Prism 4 for Windows (version 4.02, GraphPad Software Inc., San Diego, California, USA). Sigmoidal dose response curves typically have R² values >0.90 as determined by the software. EC₅₀ values calculated by the analysis program were used for comparison of bioactivity.

[0228] As shown in Figures 13 to 17 and 40, all of the generated cross-species specific bispecific single chain antibody constructs demonstrate cytotoxic activity against human MCSP D3 positive target cells elicited by stimulated human CD4/CD56 depleted PBMC or stimulated PBMC and against macaque MCSP D3 positive target cells elicited by the macaque T cell line 4119LnPx.

12. Plasma stability of MCSP and CD3 cross-species specific bispecific single chain antibodies

[0229] Stability of the generated bispecific single chain antibodies in human plasma was analyzed by incubation of the bispecific single chain antibodies in 50% human Plasma at 37°C and 4°C for 24 hours and subsequent testing of bioactivity. Bioactivity was studied in a chromium 51 (⁵¹Cr) release in vitro cytotoxicity assay using a MCSP positive CHO cell line (expressing MCSP as cloned according to example 14 or 15) as target and stimulated human CD8 positive T cells as effector cells.

[0230] EC₅₀ values calculated by the analysis program as described above were used for comparison of bioactivity of bispecific single chain antibodies incubated with 50% human plasma for 24 hours at 37°C and 4°C respectively with bispecific single chain antibodies without addition of plasma or mixed with the same amount of plasma immediately prior to the assay.

[0231] As shown in Figure 18 and Table 2 the bioactivity of the G4 H-L × I2C H-L, G4 H-L × H2C H-L and G4 H-L × F12Q H-L bispecific antibodies was not significantly reduced as compared with the controls without the addition of plasma or with addition of plasma immediately before testing of bioactivity.

Table 2: bioactivity of the bispecific antibodies without or with the addition of Plasma

Construct	Without plasma	With plasma	Plasma 37°C	Plasma 4°C
G4 H-L × I2C H-L	300	796	902	867
G4 H-L × H2C H-L	496	575	2363	1449
G4 H-L × F12Q H-L	493	358	1521	1040

13. Redistribution of circulating T cells in the absence of circulating target cells by first exposure to CD3 binding molecules directed at conventional i.e. context dependent CD3 epitopes is a major risk factor for adverse events related to the initiation of treatment

T cell redistribution in patients with B-cell Non-Hodgkin-Lymphoma (B-NHL) following initiation of treatment with the conventional CD3 binding molecule

[0232] A conventional CD19xCD3 binding molecules is a CD3 binding molecule of the bispecific tandem scFv format (Loffler (2000, Blood, Volume 95, Number 6) or WO 99/54440). It consists of two different binding portions directed at (i) CD19 on the surface of normal and malignant human B cells and (ii) CD3 on human T cells. By crosslinking CD3 on T cells with CD19 on B cells, this construct triggers the redirected lysis of normal and malignant B cells by the cytotoxic activity of T cells. The CD3 epitope recognized by such a conventional CD3 binding molecule is localized on the CD3 epsilon chain, where it only takes the correct conformation if it is embedded within the rest of the epsilon chain and held in the right position by heterodimerization of the epsilon chain with either the CD3 gamma or delta chain. Interaction of this highly context dependent epitope with a conventional CD3 binding molecule (see e.g. Loffler (2000, Blood, Volume 95, Number 6) or WO 99/54440) - even when it occurs in a purely monovalent fashion and without any crosslinking - can induce an allosteric change in the conformation of CD3 leading to the exposure of an otherwise hidden proline-rich region within the cytoplasmic domain of CD3 epsilon. Once exposed, the proline-rich region can recruit the signal transduction molecule Nck2, which is capable of triggering further intracellular signals. Although this is not sufficient for full T cell activation, which definitely requires crosslinking of several CD3 molecules on the T cell surface, e.g. by crosslinking of several anti-CD3 molecules bound to several CD3 molecules on a T cell by several CD19 molecules on the surface of a B cell, pure monovalent interaction of conventional CD3 binding molecules to their context dependent epitope on CD3 epsilon is still not inert for T cells in terms of signalling. Without being bound by theory, monovalent conventional CD3 binding molecules (known in the art) may induce some T cell reactions when infused into humans even in those cases where no circulating target cells are available for CD3 crosslinking. An important T cell reaction to the intravenous infusion of monovalent conventional CD19xCD3 binding molecule into B-NHL patients who have essentially no circulating CD19-positive B cells is the redistribution of T cells after start of treatment. It has been found in a phase I clinical trial that this T cell reaction occurs during the starting phase of intravenous CD19xCD3 binding molecule infusion in all individuals without circulating CD19-positive target B cells essentially independent of the CD19xCD3 binding molecule dose (Fig. 19). However, sudden increases in CD19xCD3 binding molecule exposure have been found to trigger virtually the same redistributional T cell reaction in these patients as the initial exposure of T cells to CD19xCD3 binding molecule at treatment start (Fig. 20 A) and even gradual increases in CD19xCD3 binding molecule exposure still can have redistributional effects on circulating T cells (Fig. 21). Moreover, it has been found that this essentially dose-independent redistributional T cell reaction in the absence of circulating target cells as triggered by conventional CD3 binding molecules like the CD19xCD3 binding molecule (e.g. disclosed in WO 99/54440) in 100% of all treated individuals is a major risk factor for adverse events related to the initiation of treatment.

[0233] According to the study protocol, patients with relapsed histologically confirmed indolent B-cell Non-Hodgkin-Lymphoma (B-NHL) including mantle cell lymphoma were recruited in an open-label, multi-center phase I interpatient dose-escalation trial. The study protocol was approved by the independent ethics committees of all participating centers and sent for notification to the responsible regulatory authority.

[0234] Measurable disease (at least one lesion ≥ 1.5 cm) as documented by CT scan was required for inclusion into the study. Patients received conventional CD19xCD3 binding molecule by continuous intravenous infusion with a portable minipump system over four weeks at constant flow rate (i.e. dose level). Patients were hospitalized during the first two weeks of treatment before they were released from the hospital and continued treatment at home. Patients without evidence of disease progression after four weeks were offered to continue treatment for further four weeks. So far six different dose levels were tested without reaching a maximum tolerated dose (MTD): 0.5, 1.5, 5, 15, 30 and 60 $\mu\text{g}/\text{m}^2/24\text{h}$. Cohorts consisted of three patients each if no adverse events defined by the study protocol as DLT (dose limiting toxicity) were observed. In case of one DLT among the first three patients the cohort was expanded to six patients, which - in the absence of a second DLT - allowed further dose escalation. Accordingly, dose levels without DLT in cohorts with 3 patients or with one DLT in cohorts with 6 patients were regarded as safe. Study treatment was stopped in all patients who developed a DLT. At 15 and 30 $\mu\text{g}/\text{m}^2/24\text{h}$ different modes of treatment initiation during the first 24h were tested in several additional cohorts: (i) Stepwise increase after 5 $\mu\text{g}/\text{m}^2/24\text{h}$ for the first 24h to 15 $\mu\text{g}/\text{m}^2/24\text{h}$ maintenance dose (patient cohort 15-step), (ii) even continuous increase of flow-rate from almost zero to 15 or 30 $\mu\text{g}/\text{m}^2/24\text{h}$ (patient cohorts 15-ramp and 30-ramp) and (iii) start with the maintenance dose from the very beginning (patient cohorts 15-flat, 30-flat and 60-flat). Patient cohorts at dose levels 0.5, 1.5 and 5 $\mu\text{g}/\text{m}^2/24\text{h}$ were all started with the maintenance dose from the very beginning (i.e. flat initiation).

[0235] Time courses of absolute B- and T-cell counts in peripheral blood were determined by four color FACS analysis as follows:

Collection of blood samples and routine analysis

[0236] In patient cohorts 15-ramp, 15-flat, 30-ramp, 30-flat and 60-flat blood samples (6 ml) were obtained before and 0.75, 2, 6, 12, 24, 30, 48 hours after start of CD19xCD3 binding molecule (as disclosed in WO 99/54440) infusion as well as on treatment days 8, 15, 17, 22, 24, 29, 36, 43, 50, 57 and 4 weeks after end of conventional CD19xCD3 binding molecule infusion using EDTA-containing Vacutainer™ tubes (Becton Dickinson) which were shipped for analysis at 4°C. In patient cohorts 15-step blood samples (6 ml) were obtained before and 6, 24, 30, 48 hours after start of CD19xCD3 binding molecule infusion as well as on treatment days 8, 15, 22, 29, 36, 43, 50, 57 and 4 weeks after end of CD19xCD3 binding molecule infusion. At dose levels 0.5, 1.5 and 5 µg/m²/24h blood samples (6 ml) were obtained before and 6, 24, 48 hours after start of CD19xCD3 binding molecule infusion as well as on treatment days 8, 15, 22, 29, 36, 43, 50, 57 and 4 weeks after end of CD19xCD3 binding molecule infusion. In some cases slight variations of these time points occurred for operational reasons. FACS analysis of lymphocyte subpopulations was performed within 24 - 48 h after blood sample collection. Absolute numbers of leukocyte subpopulations in the blood samples were determined through differential blood analysis on a CoulterCounter™ (Coulter).

Isolation of PBMC from blood samples

[0237] PBMC (peripheral blood mononuclear cells) isolation was performed by an adapted Ficoll™ gradient separation protocol. Blood was transferred at room temperature into 10 ml Leucosep™ tubes (Greiner) pre-loaded with 3 ml Biocoll™ solution (Biochrom). Centrifugation was carried out in a swing-out rotor for 15 min at 1700xg and 22°C without deceleration. The PBMC above the Biocoll™ layer were isolated, washed once with FACS buffer (PBS / 2% FBS [Foetal Bovine Serum; Biochrom]), centrifuged and resuspended in FACS buffer. Centrifugation during all wash steps was carried out in a swing-out rotor for 4 min at 800xg and 4°C. If necessary, lysis of erythrocytes was performed by incubating the isolated PBMC in 3 ml erythrocyte lysis buffer (8.29 g NH₄Cl, 1.00 g KHCO₃, 0.037 g EDTA, ad 1.0 l H₂O_{bidest}, pH 7.5) for 5 min at room temperature followed by a washing step with FACS buffer.

Staining of PBMC with fluorescence-labeled antibodies against cell surface molecules

[0238] Monoclonal antibodies were obtained from Invitrogen (1st Cat. No. MHCD1301, 2nd Cat. No. MHCD1401), Dako (5th Cat. No. C7224) or Becton Dickinson (3rd Cat. No. 555516, 4th Cat. No. 345766) used according to the manufacturers' recommendations. 5×10^5 - 1×10^6 cells were stained with the following antibody combination: anti-CD13¹ / anti-CD14² (FITC) × anti-CD56³ (PE) × anti-CD3⁴ (PerCP) × anti-CD19⁵ (APC). Cells were pelleted in V-shaped 96 well multititer plates (Greiner) and the supernatant was removed. Cell pellets were resuspended in a total volume of 100 µl containing the specific antibodies diluted in FACS buffer. Incubation was carried out in the dark for 30 min at 4°C. Subsequently, samples were washed twice with FACS buffer and cell pellets were resuspended in FACS buffer for flowcytometric analysis.

Flowcytometric detection of stained lymphocytes by FACS

[0239] Data collection was performed with a 4 color BD FACSCalibur™ (Becton Dickinson). For each measurement 1×10^4 cells of defined lymphocyte subpopulations were acquired. Statistical analysis was performed with the program CellQuest Pro™ (Becton Dickinson) to obtain lymphocyte subpopulation percentages and to classify cell surface molecule expression intensity. Subsequently, percentages of single lymphocyte subsets related to total lymphocytes (i.e. B plus T plus NK cells excluding any myeloid cells via CD13/14-staining) as determined by FACS were correlated with the lymphocyte count from the differential blood analysis to calculate absolute cell numbers of T cells (CD3⁺, CD56⁻, CD13/14⁻) and B cells (CD19⁺, CD13/14⁻).

[0240] T cell redistribution during the starting phase of conventional CD19xCD3 binding molecule (e.g. disclosed in WO 99/54440) treatment in all those patients who had essentially no circulating CD19-positive B cells at treatment start is shown in (Fig. 19). For comparison, a representative example of T cell redistribution during the starting phase of CD19xCD3 binding molecule treatment in a patient with a significant number of circulating CD19-positive B cells is shown in Fig. 22.

[0241] In both cases (i.e. essentially no or many circulating B cells) circulating T cell counts rapidly decrease upon treatment start. However, in the absence of circulating B cells T cells tend to return into the circulating blood very early, while the return of T cells into the circulating blood of those patients who have a significant number of circulating B cells at treatment start is usually delayed until these circulating B cells are depleted. Thus, the T cell redistribution patterns mainly differ in the kinetics of T cell reappearance in the circulating blood.

[0242] Assessment of efficacy based on CT scan was carried out by central reference radiology after 4 weeks of treatment and in patients receiving additional 4 weeks also after 8 weeks of treatment plus in all cases four weeks after

end of treatment. Disappearance and/or normalization in size of all known lesions (including an enlarged spleen) plus clearance of bone marrow from lymphoma cells in cases of bone marrow infiltration was counted as complete response (CR). Reduction by at least 50% from baseline of the sum of products of the two biggest diameters (SPD) of each predefined target lesion was defined as partial response (PR); a reduction by at least 25% was regarded a minimal response (MR). Progressive disease (PD) was defined as $\geq 50\%$ increase of SPD from baseline. SPD deviations from baseline between +50% and -25% were regarded as stable disease (SD).

[0243] Patient demographics, doses received and clinical outcome in 34 patients are summarized in Table 3. Clinical anti-tumor activity of the CD19xCD3 binding molecule was clearly dose dependent: Consistent depletion of circulating CD19-positive B (lymphoma) cell from peripheral blood was observed from 5 $\mu\text{g}/\text{m}^2/24\text{h}$ onwards. At 15 $\mu\text{g}/\text{m}^2/24\text{h}$ and 30 $\mu\text{g}/\text{m}^2/24\text{h}$ first objective clinical responses (PRs and CRs) were recorded as well as cases of partial and complete elimination of B lymphoma cells from infiltrated bone marrow. Finally, at 60 $\mu\text{g}/\text{m}^2/24\text{h}$ the response rate increased to 100% (PRs and CRs) and bone marrow clearance from B lymphoma cells was complete in all evaluable cases.

[0244] The CD19xCD3 binding molecule was well tolerated by the majority of patients. Most frequent adverse events of grades 1-4 in 34 patients, regardless of causality are summarized in Table 4. CD19xCD3 binding molecule-related adverse events usually were transient and fully reversible. In particular, there were 2 patients (patients # 19 and # 24 in Table 3) essentially without circulating CD19-positive B cells whose treatment was stopped early because of CNS adverse events (lead symptoms: confusion and disorientation) related to repeated T cell redistribution during the starting phase of CD19xCD3 binding molecule infusion.

[0245] One of these patients (#19) was in cohort 15-step. He received 5 $\mu\text{g}/\text{m}^2/24\text{h}$ CD19xCD3 binding molecule for the first 24h followed by sudden increase to 15 $\mu\text{g}/\text{m}^2/24\text{h}$ maintenance dose. The corresponding T cell redistribution pattern shows that circulating T cell counts rapidly decreased upon start of infusion at 5 $\mu\text{g}/\text{m}^2/24\text{h}$ followed by early reappearance of T cells in the circulating blood essentially without circulating CD19-positive B cells. As a consequence, the peripheral T cell counts had fully recovered when the CD19xCD3 binding molecule dose was increased after 24h from 5 to 15 $\mu\text{g}/\text{m}^2/24\text{h}$. Therefore the dose step could trigger a second episode of T cell redistribution as shown in Fig. 20 A. This repeated T cell redistribution was related with CNS side effects (lead symptoms: confusion and disorientation) in this patient, which led to the stop of infusion. The relationship between repeated T cell redistribution and such CNS adverse events was also observed in previous phase I clinical trials in B-NHL patients who received CD19xCD3 binding molecule (e.g. disclosed in WO 99/54440) as repeated bolus infusion for 2 to 4 hours each usually followed by 2 days of treatment free interval (Fig. 20 B). Every single bolus infusion triggered one episode of T cell redistribution consisting of a fast decrease in circulating T cell counts and T cell recovery prior to the next bolus infusion. In total, CNS adverse events related to repeated T cell redistribution were observed in 5 out of 21 patients. Fig. 20 B shows the representative example of one patient from the bolus infusion trials, who developed CNS symptoms after the third episode of T cell redistribution. Typically, patients with CNS adverse events in the bolus infusion trials also had low circulating B cell counts.

[0246] The second patient (#24) from the continuous infusion trial, whose treatment was stopped early because of CNS adverse events (lead symptoms: confusion and disorientation) related to repeated T cell redistribution during the starting phase of CD19xCD3 binding molecule infusion, was in cohort 15-flat. By mistake, this patient received an CD19xCD3 binding molecule infusion without additional HSA as required for stabilization of the drug. The resulting uneven drug flow triggered repeated episodes of T cell redistribution instead of only one (Fig. 23 A) with the consequence that the infusion had to be stopped because of developing CNS symptoms. Yet, when the same patient was restarted correctly with CD19xCD3 binding molecule solution containing additional HSA for drug stabilization (e.g. disclosed in WO 99/54440), no repeated T cell redistribution was observed and the patient did not again develop any CNS symptoms (Fig. 23 B). Because this patient also had essentially no circulating B cells, the circulating T cells could react with fast redistribution kinetics even to subtle changes in drug exposure as observed. The CNS adverse events related to T cell redistribution in patients who have essentially no circulating target cells can be explained by a transient increase of T cell adhesiveness to the endothelial cells followed by massive simultaneous adhesion of circulating T cells to the blood vessel walls with a consecutive drop of T cell numbers in the circulating blood as observed. The massive simultaneous attachment of T cells to the blood vessel walls can cause an increase in endothelial permeability and endothelial cell activation. The consequences of increased endothelial permeability are fluid shifts from the intravascular compartment into interstitial tissue compartments including the CNS interstitium. Endothelial cell activation by attached T cells can have procoagulatory effects (Monaco et al. J Leukoc Biol 71 (2002) 659-668) with possible disturbances in blood flow (including cerebral blood flow) particularly with regard to capillary microcirculation. Thus, CNS adverse events related to T cell redistribution in patients essentially without circulating target cells can be the consequence of capillary leak and/or disturbances in capillary microcirculation through adherence of T cells to endothelial cells. The endothelial stress caused by one episode of T cell redistribution is tolerated by the majority of patients, while the enhanced endothelial stress caused by repeated T cell redistribution frequently causes CNS adverse events. More than one episode of T cell redistribution may be less risky only in patients who have low baseline counts of circulating T cells. However, also the limited endothelial stress caused by one episode of T cell redistribution can cause CNS adverse events in rare cases of increased susceptibility for such events as observed in 1 out of 21 patients in the bolus infusion trials with the CD19xCD3

binding molecule.

[0247] Without being bound by theory, the transient increase of T cell adhesiveness to the endothelial cells in patients who have essentially no circulating target cells can be explained as T cell reaction to the monovalent interaction of a conventional CD3 binding molecule, like the CD19xCD3 binding molecule (e.g. WO 99/54440), to its context dependent epitope on CD3 epsilon resulting in an allosteric change in the conformation of CD3 followed by the recruitment of Nck2 to the cytoplasmic domain of CD3 epsilon as described above. As Nck2 is directly linked to integrins via PINCH and ILK (Fig 28), recruitment of Nck2 to the cytoplasmic domain of CD3 epsilon following an allosteric change in the conformation of CD3 through binding of a conventional CD3 binding molecule, like the CD19xCD3 binding molecule, to its context dependent epitope on CD3 epsilon, can increase the adhesiveness of T cells to endothelial cells by transiently switching integrins on the T cell surface into their more adhesive isoform via inside-out-signalling.

Table 3. Patient demographics and clinical outcome

Cohort	Patient	Age/ Sex	Disease (Ann Arbor Classification)	Dose Level [mg/m ² /Day]	Clearance of Bone Marrow	Best Response* (CR Duration in Months or Weeks)
1	1	71/m	IC, Binet C	0.0005	None	SD
	2	67/f	MCL, Stage IV/A/E	0.0005	n.d.	PD
	3	67/m	CLL, Stage IV/B/E	0.0005	n.d.	MR
2	4	69/m	MCL, Stage IV/B	0.0015	n.i.	SD
	5	49/m	MCL, Stage IV/A/S	0.0015	n.d.	SD
	6	711m	MCL, Stage IV/B/E	0.0015	n.i.	PD
	7	171m	MCL, Stage IV/B/E/S	0.0015	n.i.	SD
	8	65/m	CLL, Stage IV/B/E/S	0.0015	n.d.	PD
	9	75/m	FL, Stage II/B	0.0015	n.i.	SD
3	10	58/m	MCL, Stage III/B/S	0.005	n.i.	PD
	11	68/f	FL, Stage IV/B	0.005	n.d.	SD
	12	65/m	MCL, Stage III/A/E	0.005	n.i.	SD
4 ^a	13	60/m	SLL, Stage IV/B/S	0.015	Complete	PR
	14	73/m	MCL, Stage II/A/E	0.015	n.i.	SD
	15	44/m	FL, Stage IV/B/E/S	0.015	Partial	PR
	16	61/m	FL, Stage IV/A/S	0.015	Complete	CR (7mo)
	17	67/m	MZL, Stage IV/B/S	0.015	n.i.	n.e.
	18	64/m	FL, Stage IV/A/E	0.015	n.i.	PD
	19	75/m	MCL, Stage III/A	0.015	n.i.	n.e.
	20	65/f	FL; Stage III/A	0.015	n.i.	SD
	21	60/m	MCL, Stage IV/A/E	0.015	None	SD
	22	67/f	FL, Stage IV/B	0.015	Complete	MR
	23	67/m	DLBCL, Stage III/B	0.015	n.i.	n.e.
	24	65/f	FL, Stage III/A	0.015	n.d.	SD
	25	74/f	WD, Stage IV/B	0.015	Partial	SD
5	26	67/m	MCL, Stage IV/A	0.03	Complete	SD
	27	48/m	FL, Stage III/A	0.03	n.i.	PD
	28	58/m	MCL, Stage III/A	0.03	n.i.	CR (10mo+)

(continued)

Cohort	Patient	Age/ Sex	Disease (Ann Arbor Classification)	Dose Level [mg/m ² /Day]	Clearance of Bone Marrow	Best Response* (CR Duration in Months or Weeks)
	29	45/f	MCL, Stage IV/B	0.03	Partial	PD
	30	59/m	MZL, Stage III/A	0.03	n.i.	n.e.
	31	431m	FL, Stage III/A	0.03	n.i.	MR
6	32	72/m	MCL, Stage IV/A	0.06	Complete	PR
	33	55/m	MCL, Stage IV/B	0.06	Complete	CR (4mo+)
	34	52/m	FL, Stage IV/A	0.06	n.i.	CR^b (1w+)
<p>*Centrally confirmed complete (CR) and partial (PR) responses by Cheson criteria in bold; MR, minimal response (≥25 to <50%); SD, stable disease; PD, progressive disease; duration from first documentation of response in parentheses; + denotes an ongoing response</p> <p>^aCohort 4 was expanded to study three different schedules of treatment initiation ^bPR after 8 weeks of treatment that turned into a CR after an additional treatment cycle of 4 weeks at the same dose following 7 weeks of treatment free interval</p> <p>n.e.: not evaluable, because of treatment period <7 d</p> <p>n.d.: not determined (infiltrated, but no second biopsy performed at end of treatment)</p> <p>n.i.: not infiltrated at start of treatment</p>						

Table 4. Incidence of adverse events observed during treatment

Adverse events regardless of relationship, occurring in ≥ 3 patients (N=34)		Grade 1-4 N (%)	Grade 3-4 N (%)
Pyrexia		22 (64.7)	2 (5.9)
Leukopenia		21 (61.8)	11 (32.4)
Lymphopenia		21 (61.8)	21 (61.8)
Coagulopathy (increase in D-dimers)		16 (47.1)	6 (17.6)
Enzyme abnormality (AP, LDH, CRP)		16 (47.1)	10 (29.4)
Hepatic function abnormality (ALT, AST, GGT)		16 (47.1)	1 (2.9)
Anaemia		13 (38.2)	5 (14.7)
Chills		13 (38.2)	0 (0.0)
Headache		12 (35.3)	1 (2.9)
Hypokalaemia		12 (35.3)	2 (5.9)
Thrombocytopenia		12 (35.3)	6 (17.6)
Weight increased		12 (35.3)	0 (0.0)
Hyperglycaemia		11 (32.4)	2 (5.9)
Neutropenia		11 (32.4)	8 (23.5)
Haematuria		10 (29.4)	0 (0.0)
Oedema peripheral		10 (29.4)	2 (5.9)
Anorexia		9 (26.5)	1 (2.9)
Diarrhoea		9 (26.5)	0 (0.0)
Weight decreased		9 (26.5)	0 (0.0)
Fatigue		8 (23.5)	1 (2.9)

(continued)

Adverse events regardless of relationship, occurring in ≥ 3 patients (N=34)		Grade 1-4 N (%)	Grade 3-4 N (%)
5	Proteinuria	8 (23.5)	0 (0.0)
	Hypocalcaemia	7 (20.6)	2 (5.9)
	Pancreatic enzyme abnormality	7 (20.6)	0 (0.0)
	Cough	6 (17.6)	0 (0.0)
10	Dyspnoea	6 (17.6)	0 (0.0)
	Back pain	5 (14.7)	0 (0.0)
	Catheter site pain	5 (14.7)	0 (0.0)
15	Hyperbilirubinaemia	5 (14.7)	2 (5.9)
	Hypoalbuminaemia	5 (14.7)	0 (0.0)
	Hypogammaglobulinaemia	5 (14.7)	1 (2.9)
	Hypoproteinaemia	5 (14.7)	0 (0.0)
20	Pleural effusion	5 (14.7)	1 (2.9)
	Vomiting	5 (14.7)	0 (0.0)
	Asthenia	4 (11.8)	1 (2.9)
25	Confusional state	4 (11.8)	0 (0.0)
	Constipation	4 (11.8)	0 (0.0)
	Dizziness	4 (11.8)	0 (0.0)
	Hypertension	4 (11.8)	0 (0.0)
30	Hyponatraemia	4 (11.8)	2 (5.9)
	Mucosal dryness	4 (11.8)	0 (0.0)
	Muscle spasms	4 (11.8)	0 (0.0)
35	Nausea	4 (11.8)	0 (0.0)
	Night sweats	4 (11.8)	0 (0.0)
	Abdominal pain	3 (8.8)	1 (2.9)
	Ascites	3 (8.8)	0 (0.0)
40	Hypercoagulation	3 (8.8)	0 (0.0)
	Hyperhidrosis	3 (8.8)	0 (0.0)
	Hypoglobulinaemia	3 (8.8)	0 (0.0)
45	Insomnia	3 (8.8)	0 (0.0)
	Liver disorder	3 (8.8)	1 (2.9)
	Nasopharyngitis	3 (8.8)	0 (0.0)
50	Pruritus	3 (8.8)	0 (0.0)

[0248] Abbreviations used are: AE, adverse event; AP, alkaline phosphatase; LDH, lactate dehydrogenase; CRP, C-reactive protein; ALT, alanine transaminase; AST, aspartate transaminase; GGT, gamma-glutamyl transferase; AE data from the additional treatment cycle of patient 34 not yet included.

[0249] As explained above, conventional CD3 binding molecules (e.g. disclosed in WO 99/54440) capable of binding to a context-dependent epitope, though functional, lead to the undesired effect of T cell redistribution in patients causing CNS adverse events. In contrast, binding molecules of the present invention, by binding to the context-independent N-terminal 1-27 amino acids of the CD3 epsilon chain, do not lead to such T cell redistribution effects. As a consequence,

the CD3 binding molecules of the invention are associated with a better safety profile compared to conventional CD3 binding molecules.

14. Bispecific CD3 binding molecules of the invention inducing T cell mediated target cell lysis by recognizing a surface target antigen deplete target antigen positive cells in vivo

A bispecific CD3 binding molecule of the invention recognizing CD33 as target antigen depletes CD33-positive circulating monocytes from the peripheral blood of cynomolgus monkeys

[0250] CD33-AF5 VH-VL \times I2C VH-VL (amino acid sequence: SEQ ID NO.267) was produced by expression in CHO cells using the coding nucleotide sequence SEQ ID NO. 268. The coding sequences of (i) an N-terminal immunoglobulin heavy chain leader comprising a start codon embedded within a Kozak consensus sequence and (ii) a C-terminal His₆-tag followed by a stop codon were both attached in frame to the nucleotide sequence SEQ ID NO 268 prior to insertion of the resulting DNA-fragment as obtained by gene synthesis into the multiple cloning site of the expression vector pEF-DHFR (Raum et al. Cancer Immunol Immunother 50 (2001) 141-150). Stable transfection of DHFR-deficient CHO cells, selection for DHFR-positive transfectants secreting the CD3 binding molecule CD33-AF5 VH-VL \times I2C VH-VL into the culture supernatant and gene amplification with methotrexat for increasing expression levels were carried out as described (Mack et al. Proc. Natl. Acad. Sci. USA 92 (1995) 7021-7025). The analytical SEC-profile of CD33-AF5 VH-VL \times I2C VH-VL for use in cynomolgus monkeys revealed that the test material almost exclusively consisted of monomer. The potency of the test material was measured in a cytotoxicity assay as described in example 16.5 using CHO cells transfected with cynomolgus CD33 as target cells and the macaque T cell line 4119LnPx as source of effector cells (FIG. 25). The concentration of CD33-AF5 VH-VL \times I2C VH-VL required for half-maximal target cell lysis by the effector T cells (EC50) was determined to be 2.7 ng/ml.

[0251] Young (approx. 3 years old) adult cynomolgus monkeys (*Macaca fascicularis*) were treated by continuous intravenous infusion of CD3 binding molecule CD33-AF5 VH-VL \times I2C VH-VL at different flow-rates (i.e. dose levels) to study depletion of circulating CD33-positive monocytes from the peripheral blood. This situation is equivalent to the treatment with the conventional CD3 binding molecule CD19xCD3 (specific for CD19 on B cells and CD3 on T cells) of those B-NHL patients, who have circulating CD19-positive target B cells (see e.g. WO99/54440). Depletion of circulating CD19-positive target B cells from the peripheral blood had turned out as a valid surrogate for the general clinical efficacy of the conventional CD3 binding molecule (CD19xCD3 as provided in WO99/54440) in patients with CD19-positive B-cell malignomas like B-NHL. Likewise, depletion of circulating CD33-positive monocytes from the peripheral blood is regarded as a valid surrogate of the general clinical efficacy of CD33-directed bispecific CD3 binding molecules of the invention like CD33-AF5 VH-VL \times I2C VH-VL in patients with CD33-positive myeloid malignomas like AML (acute myeloid leukemia).

[0252] Continuous infusion was carried out according to the Swivel method as follows: The monkeys are catheterized via the vena femoralis into the vena cava caudalis using a vein catheter. The catheter is tunneled subcutaneously to the dorsal shoulder region and exteriorized at the caudal scapula. Then a tube is passed through a jacket and a protection spring. The jacket is fastened around the animal and the catheter, via the tube, is connected to an infusion pump.

[0253] Administration solution (1.25 M lysine, 0.1% tween 80, pH 7) without test material was infused continuously at 48 ml/24h for 7 days prior to treatment start to allow acclimatization of the animals to the infusion conditions. Treatment was started by adding CD33-AF5 VH-VL \times I2C VH-VL test material to the administration solution at the amount required for each individual dose level to be tested (i.e. flow rate of CD33-AF5 VH-VL \times I2C VH-VL). The infusion reservoir was changed every day throughout the whole acclimatization and treatment phase. Planned treatment duration was 7 days except for the 120 μ g/m²/24h dose level, where animals received 14 days of treatment.

[0254] Time courses of absolute counts in circulating T cells and CD33-positive monocytes were determined by 4- or 3-colour FACS analysis, respectively.

Collection of blood samples and routine analysis

[0255] Blood samples (1 ml) were obtained before and 0.75, 2, 6, 12, 24, 30, 48, 72 hours after start of continuous infusion with MCSP-G4 VH-VL \times I2C VH-VL as well as after 7 and 14 days (and after 9 days at the 120 μ g/m²/24h dose level) of treatment using EDTA-containing Vacutainer™ tubes (Becton Dickinson) which were shipped for analysis at 4°C. In some cases slight variations of these time points occurred for operational reasons. FACS analysis of lymphocyte subpopulations was performed within 24 - 48 h after blood sample collection. Absolute numbers of leukocyte subpopulations in the blood samples were determined through differential blood analysis in a routine veterinary lab.

Isolation of PBMC from blood samples

[0256] PBMC (peripheral blood mononuclear cells) were isolated in analogy to the protocol described in example 13, above, with adaptations of the used volumes.

Staining of PBMC with fluorescence-labeled antibodies against cell surface molecules

[0257] Monoclonal antibodies reactive with cynomolgus antigens were obtained from Becton Dickinson (¹Cat. No. 345784, ²Cat. No. 556647, ³Cat. No. 552851, ⁶Cat. No. 557710), Beckman Coulter (⁴Cat. No. IM2470) and Miltenyi (⁵Cat. No. 130-091-732) and used according to the manufacturers' recommendations. 5×10^5 - 1×10^6 cells were stained with the following antibody combinations: anti-CD14¹ (FITC) \times anti-CD56² (PE) \times anti-CD3³ (PerCP) \times anti-CD19⁴ (APC) and anti-CD14¹ (FITC) \times anti-CD33⁵ (PE) \times anti-CD16⁶ (Alexa Fluor 647TM). Additional steps were performed as described in example 13, above.

Flowcytometric detection of stained lymphocytes by FACS

[0258] Data collection was performed with a 4 color BD FACSCaliburTM (Becton Dickinson). For each measurement 1×10^4 cells of defined lymphocyte subpopulations were acquired. Statistical analysis was performed with the program CellQuest ProTM (Becton Dickinson) to obtain lymphocyte subpopulation percentages and to classify cell surface molecule expression intensity. Subsequently, percentages of single lymphocyte subsets related to total lymphocytes (i.e. B plus T plus NK cells excluding myeloid cells via CD14-staining) as determined by FACS were correlated with the lymphocyte count from the differential blood analysis to calculate absolute cell numbers of T cells (CD3⁺, CD56⁻, CD14⁻). Absolute numbers of CD33-positive monocytes were calculated by multiplying the monocyte counts from the differential blood analysis with the corresponding ratios of CD33-positive monocytes (CD33⁺, CD14⁺) to all monocytes (CD14⁺) as determined by FACS.

[0259] The percentage compared to baseline (i.e. 100%) of absolute circulating CD33-positive monocyte counts at the end of treatment with CD33-AF5 VH-VL \times I2C VH-VL in 4 cohorts of 2 cynomolgus monkeys with inter-cohort dose escalation from 30 over 60 and 240 to 1000 $\mu\text{g}/\text{m}^2/24\text{h}$ are shown in FIG 26 A.

[0260] As shown in FIG 26 A, continuous intravenous infusion of CD33-AF5 VH-VL \times I2C VH-VL induces depletion of circulating CD33-positive monocytes in a dose-dependent manner. While there was still no detectable depletion of circulating CD33-positive monocytes at 30 $\mu\text{g}/\text{m}^2/24\text{h}$, a first trend towards a reduction of CD33-positive monocyte counts became visible at 60 $\mu\text{g}/\text{m}^2/24\text{h}$ after 7 days of treatment. At 240 $\mu\text{g}/\text{m}^2/24\text{h}$ circulating CD33-positive monocytes were almost completely depleted from the peripheral blood after 3 days of treatment. This was reached even faster at 1000 $\mu\text{g}/\text{m}^2/24\text{h}$, where depletion of the circulating CD33-positive monocytes from the peripheral blood was completed already after 1 day of treatment. This finding was confirmed by the results shown in Figure 26 B demonstrating depletion of circulating CD33-positive monocytes by two thirds and 50% compared to the respective baseline in two cynomolgus monkeys treated by continuous infusion with CD33-AF5 VH-VL \times I2C VH-VL at 120 $\mu\text{g}/\text{m}^2/24\text{h}$ for 14 days.

[0261] This outcome is a clear signal clinical efficacy of the CD3 binding molecules of the invention in general and of bispecific CD33-directed CD3 binding molecules of the invention for the treatment of CD33-positive malignomas like AML in particularly. Moreover, the T cell redistribution during the starting phase of treatment with CD33-AF5 VH-VL \times I2C VH-VL in the presence of circulating target cells (i.e. CD33-positive monocytes) seems to be less pronounced than T cell redistribution during the starting phase of treatment with conventional CD19 \times CD3 constructs, as described in WO99/54440 in B-NHL patients with a significant number of circulating target cells (i.e. CD19-positive B cells) as shown in Fig 22. While T cells disappear completely from the circulation upon start of CD19 \times CD3 infusion and do not reappear until the circulating CD19-positive target B cells are depleted from the peripheral blood (FIG 22), initial disappearance of circulating T cells is incomplete upon infusion start with CD33-AF5 VH-VL \times I2C VH-VL and T cell counts recover still during the presence of circulating CD33-positive target cells (FIG 26 B). This confirms that CD3 binding molecules of the invention (directed against and generated against an epitope of human and non-chimpanzee primates CD3 ϵ (epsilon) chain and being a part or fragment or the full length of the amino acid sequence as provided in SEQ ID Nos. 2, 4, 6, or 8) by recognizing a context-independent CD3 epitope show a more favorable T cell redistribution profile than conventional CD3 binding molecules recognizing a context-dependent CD3 epitope, like the binding molecules provided in WO99/54440.

15. CD3 binding molecules of the invention directed at essentially context independent CD3 epitopes by inducing less redistribution of circulating T cells in the absence of circulating target cells reduce the risk of adverse events related to the initiation of treatment

Reduced T cell redistribution in cynomolgus monkeys following initiation of treatment with a representative cross-species specific CD3 binding molecule of the invention

[0262] MCSP-G4 VH-VL \times I2C VH-VL (amino acid sequence: SEQ ID NO. 193) was produced by expression in CHO cells using the coding nucleotide sequence SEQ ID NO. 194. The coding sequences of (i) an N-terminal immunoglobulin heavy chain leader comprising a start codon embedded within a Kozak consensus sequence and (ii) a C-terminal His6-tag followed by a stop codon were both attached in frame to the nucleotide sequence SEQ ID NO. 194 prior to insertion of the resulting DNA-fragment as obtained by gene synthesis into the multiple cloning site of the expression vector pEF-DHFR (Raum et al. Cancer Immunol Immunother 50 (2001) 141-150). Stable transfection of DHFR-deficient CHO cells, selection for DHFR-positive transfectants secreting the CD3 binding molecule MCSP-G4 VH-VL \times I2C VH-VL into the culture supernatant and gene amplification with methotrexat for increasing expression levels were carried out as described (Mack et al. Proc. Natl. Acad. Sci. USA 92 (1995) 7021-7025). Test material for treatment of cynomolgus monkeys was produced in a 200-liter fermenter. Protein purification from the harvest was based on IMAC affinity chromatography targeting the C-terminal His6-tag of MCSP-G 4 V H-VL \times I2C VH-VL followed by preparative size exclusion chromatography (SEC). The total yield of final endotoxin-free test material was 40 mg. The test material consisted of 70 % monomer, 30% dimer and a small contamination of higher multimer. The potency of the test material was measured in a cytotoxicity assay as described in example 11 using CHO cells transfected with cynomolgus MCSP as target cells and the macaque T cell line 4119LnPx as source of effector cells (FIG 27). The concentration of MCSP-G4 VH-VL \times I2C VH-VL required for half-maximal target cell lysis by the effector T cells (EC50) was determined to be 1.9 ng/ml.

[0263] Young (approx. 3 years old) adult cynomolgus monkeys (*Macaca fascicularis*) were treated by continuous intravenous infusion of CD3 binding molecule MCSP-G4 VH-VL \times I2C VH-VL at different flow-rates (i.e. dose levels) to study redistribution of circulating T cells following initiation of treatment in the absence of circulating target cells. Although the CD3 binding molecule MCSP-G4 VH-VL \times I2C VH-VL can recognize both cynomolgus MCSP and cynomolgus CD3, there are no circulating blood cells expressing MCSP. Therefore, the only interaction possible in the circulating blood is binding of the CD3-specific arm of MCSP-G4 VH-VL \times I2C VH-VL to CD3 on T cells. This situation is equivalent to the treatment with the conventional CD3 binding molecule (CD19 \times CD3 binding molecule specific for CD19 on B cells and CD3 on T cells) of those B-NHL patients, who have no circulating CD19-positive target B cells as described in example 13.

[0264] Continuous infusion was carried out according to the Swivel method as follows: The monkeys are catheterized via the vena femoralis into the vena cava caudalis using a vein catheter. The catheter is tunneled subcutaneously to the dorsal shoulder region and exteriorized at the caudal scapula. Then a tube is passed through a jacket and a protection spring. The jacket is fastened around the animal and the catheter, via the tube, is connected to an infusion pump.

[0265] Administration solution (1.25 M lysine, 0.1% tween 80, pH 7) without test material was infused continuously at 48 ml/24h for 7 days prior to treatment start to allow acclimatization of the animals to the infusion conditions. Treatment was started by adding MCSP-G4 VH-VL \times I2C VH-VL test material to the administration solution at the amount required for each individual dose level to be tested (i.e. flow rate of MCSP-G4 VH-VL \times I2C VH-VL). The infusion reservoir was changed every day throughout the whole acclimatization and treatment phase. Treatment duration was 7 days.

[0266] Time courses of absolute T-cell counts in peripheral blood were determined by four color FACS analysis as follows:

Collection of blood samples and routine analysis

[0267] Blood samples (1 ml) were obtained before and 0.75, 2, 6, 12, 24, 30, 48, 72 hours after start of continuous infusion with MCSP-G4 VH-VL \times I2C VH-VL as well as after 7 days of treatment using EDTA-containing Vacutainer™ tubes (Becton Dickinson) which were shipped for analysis at 4°C. In some cases slight variations of these time points occurred for operational reasons. FACS analysis of lymphocyte subpopulations was performed within 24 - 48 h after blood sample collection. Absolute numbers of leukocyte subpopulations in the blood samples were determined through differential blood analysis in a routine veterinary lab.

Isolation of PBMC from blood samples

[0268] PBMC were isolated in analogy to the protocol described in example 13, above, with adaptations of the used volumes.

Staining of PBMC with fluorescence-labeled antibodies against cell surface molecules

[0269] Monoclonal antibodies reactive with cynomolgus antigens were obtained from Becton Dickinson (¹Cat. No. 345784, ²Cat. No. 556647, ³Cat. No. 552851) and Beckman Coulter (⁴Cat. No. IM2470) used according to the manufacturers' recommendations. 5×10^5 - 1×10^6 cells were stained with the following antibody combination: anti-CD14¹ (FITC) \times anti-CD56² (PE) \times anti-CD3³ (PerCP) \times anti-CD19⁴ (APC). Additional steps were performed as described in example 13, above.

Flowcytometric detection of stained lymphocytes by FACS

[0270] Data collection was performed with a 4 color BD FACSCalibur™ (Becton Dickinson). For each measurement 1×10^4 cells of defined lymphocyte subpopulations were acquired. Statistical analysis was performed with the program CellQuest Pro™ (Becton Dickinson) to obtain lymphocyte subpopulation percentages and to classify cell surface molecule expression intensity. Subsequently, percentages of single lymphocyte subsets related to total lymphocytes (i.e. B plus T plus NK cells excluding myeloid cells via CD14-staining) as determined by FACS were correlated with the lymphocyte count from the differential blood analysis to calculate absolute cell numbers of T cells (CD3⁺, CD56⁻, CD14⁻).

[0271] T cell redistribution during the starting phase of treatment with MCSP-G4 VH-VL \times I2C VH-VL in cynomolgus monkeys at dose levels of 60, 240 and 1000 $\mu\text{g}/\text{m}^2/24\text{h}$ is shown in Fig 28. These animals showed no signs at all of any T cell redistribution during the starting phase of treatment, i.e. T cell counts rather increased than decreased upon treatment initiation. Given that T cell redistribution is consistently observed in 100% of all patients without circulating target cells, upon treatment initiation with the conventional CD3 binding molecule (e.g. CD19xCD3 construct as described in WO 99/54440) against a context dependent CD3 epitope, it was demonstrated that substantially less T cell redistribution in the absence of circulating target cells upon treatment initiation can be observed with a CD3 binding molecule of the invention directed and generated against an epitope of human or non-chimpanzee primate CD3 epsilon chain as defined by the amino acid sequence of any one of SEQ ID NOs: 2, 4, 6, or 8 or a fragment thereof. This is in clear contrast to CD3-binding molecules directed against a context-dependent CD3 epitope, like the constructs described in WO 99/54440. The binding molecules against context-independent CD3 epitopes, as (inter alia) provided in any one of SEQ ID NOs: 2, 4, 6, or 8 (or fragments of these sequences) provide for this substantially less (detrimental and non-desired) T cell redistribution. Because T cell redistribution during the starting phase of treatment with CD3 binding molecules is a major risk factor for CNS adverse events, the CD3 binding molecules provided herein and capable of recognizing a context independent CD3 epitope have a substantial advantage over the CD3 binding molecules known in the art and directed against context-dependent CD3 epitopes. Indeed none of the cynomolgus monkeys treated with MCSP-G4 VH-VL \times I2C VH-VL showed any signs of CNS symptoms.

[0272] The context-independence of the CD3 epitope is provided in this invention and corresponds to the first 27 N-terminal amino acids of CD3 epsilon) or fragments of this 27 amino acid stretch. This context-independent epitope is taken out of its native environment within the CD3 complex and fused to heterologous amino acid sequences without loss of its structural integrity. Anti-CD3 binding molecules as provided herein and generated (and directed) against a context-independent CD3 epitope provide for a surprising clinical improvement with regard to T cell redistribution and, thus, a more favorable safety profile. Without being bound by theory, since their CD3 epitope is context-independent, forming an autonomous self-sufficient subdomain without much influence on the rest of the CD3 complex, the CD3 binding molecules provided herein induce less allosteric changes in CD3 conformation than the conventional CD3 binding molecules (like molecules provided in WO 99/54440), which recognize context-dependent CD3 epitopes like molecules provided in WO 99/54440. As a consequence (again without being bound by theory), the induction of intracellular Nck2 recruitment by the CD3 binding molecules provided herein is also reduced resulting in less isoform switch of T cell integrins and less adhesion of T cells to endothelial cells. It is preferred that preparations of CD3 binding molecules of the invention (directed against and generated against a context-independent epitope as defined herein) essentially consists of monomeric molecules. These monomeric molecules are even more efficient (than dimeric or multimeric molecules) in avoiding T cell redistribution and thus the risk of CNS adverse events during the starting phase of treatment.

16. Generation and characterization of CD33 and CD3 cross-species specific bispecific single chain molecules**16.1. Generation of CHO cells expressing human CD33**

[0273] The coding sequence of human CD33 as published in GenBank (Accession number NM_001772) was obtained by gene synthesis according to standard protocols. The gene synthesis fragment was designed as to contain first a Kozak site for eukaryotic expression of the construct, followed by a 19 amino acid immunoglobulin leader peptide, followed in frame by the coding sequence of the mature human CD33 protein, followed in frame by the coding sequence of serine glycine dipeptide, a histidines-tag and a stop codon (the cDNA and amino acid sequence of the construct is

listed under SEQ ID Nos 305 and 306). The gene synthesis fragment was also designed as to introduce restriction sites at the beginning and at the end of the fragment. The introduced restriction sites, EcoRI at the 5' end and Sall at the 3' end, were utilised in the following cloning procedures. The gene synthesis fragment was cloned via EcoRI and Sall into a plasmid designated pEF-DHFR (pEF-DHFR is described in Raum et al. Cancer Immunol Immunother 50 (2001) 141-150) following standard protocols. The aforementioned procedures were carried out according to standard protocols (Sambrook, Molecular Cloning; A Laboratory Manual, 3rd edition, Cold Spring Harbour Laboratory Press, Cold Spring Harbour, New York (2001)). A clone with sequence-verified nucleotide sequence was transfected into DHFR deficient CHO cells for eukaryotic expression of the construct. Eukaryotic protein expression in DHFR deficient CHO cells (ATCC No. CRL 9096) was performed as described by Kaufmann R.J. (1990) Methods Enzymol. 185, 537-566. Gene amplification of the construct was induced by increasing concentrations of methothrexate (MTX) to a final concentration of up to 20 nM MTX.

16.2. Generation of CHO cells expressing the extracellular domain of macaque CD33

[0274] The cDNA sequence of macaque CD33 was obtained by a set of 3 PCRs on cDNA from macaque monkey bone marrow prepared according to standard protocols. The following reaction conditions: 1 cycle at 94°C for 3 minutes followed by 35 cycles with 94°C for 1 minute, 53°C for 1 minute and 72°C for 2 minutes followed by a terminal cycle of 72°C for 3 minutes and the following primers were used:

1. forward primer:

5'-gaggaattcaccatgccgctgctgctactgctgccctgctgtgggcagggccctggctatgg-3' (SEQ ID No. 369)
reverse primer: 5'-gattgtaactgtatttggtacttcc-3' (SEQ ID No. 370)

2. forward primer: 5'-attccgcctcctgggatcc-3' (SEQ ID No. 371)

reverse primer: 5'-gcataggagacattgagctggatgg-3' (SEQ ID No. 372)

3. forward primer: 5'-gcaccaacctgacctgtcagg-3' (SEQ ID No. 373)

reverse primer: 5'-agtgggtcgactcactgggtcctgacctctgagtattcg-3' (SEQ ID No. 374)

[0275] Those PCRs generate three overlapping fragments, which were isolated and sequenced according to standard protocols using the PCR primers, and thereby provided a portion of the cDNA sequence of macaque CD33 from the second nucleotide of codon +2 to the third nucleotide of codon +340 of the mature protein. To generate a construct for expression of macaque CD33 a cDNA fragment was obtained by gene synthesis according to standard protocols (the cDNA and amino acid sequence of the construct is listed under SEQ ID Nos 307 and 308). In this construct the coding sequence of macaque CD33 from amino acid +3 to +340 of the mature CD33 protein was fused into the coding sequence of human CD33 replacing the human coding sequence of the amino acids +3 to +340. The gene synthesis fragment was also designed as to contain a Kozak site for eukaryotic expression of the construct and restriction sites at the beginning and the end of the fragment containing the cDNA coding for essentially the whole extracellular domain of macaque CD33, the macaque CD33 transmembrane domain and a macaque-human chimeric intracellular CD33 domain. The introduced restriction sites XbaI at the 5' end and Sall at the 3' end, were utilised in the following cloning procedures. The gene synthesis fragment was then cloned via XbaI and Sall into a plasmid designated pEF-DHFR (pEF-DHFR is described in Raum et al. Cancer Immunol Immunother 50 (2001) 141-150). A sequence verified clone of this plasmid was used to transfect CHO/dhfr- cells as described above.

16.3. Generation of CD33 and CD3 cross-species specific bispecific antibody molecules

Cloning of cross-species specific binding molecules

[0276] Generally, bispecific antibody molecules, each comprising a domain with a binding specificity cross-species specific for human and non-chimpanzee primate CD3 epsilon as well as a domain with a binding specificity cross-species specific for human and non-chimpanzee primate CD33, were designed as set out in the following Table 5:

Table 5: Formats of anti-CD3 and anti-CD33 cross-species specific bispecific molecules

SEQ ID (nucl/prot)	Formats of protein constructs (N → C)
276/275	AH11HLxH2CHL
258/257	AH3HLxH2CHL

(continued)

SEQ ID (nucl/prot)	Formats of protein constructs (N → C)
270/269	AC8HLxH2CHL
264/263	AF5HLxH2CHL
288/287	F2HLxH2CHL
300/299	E11HLxH2CHL
282/281	B3HLxH2CHL
294/293	B10HLxH2CHL
278/277	AH11HLxF12QHL
260/259	AH3HLxF12QHL
272/271	AC8HLxF12QHL
266/265	AF5HLxF12QHL
290/289	F2HLxF12QHL
302/301	E11HLxF12QHL
284/283	B3HLxF12QHL
296/295	B10HLxF12QHL
280/279	AH11HLxI2CHL
262/261	AH3HLxI2CHL
274/273	AC8HLxI2CHL
268/267	AF5HLxI2CHL
292/291	F2HLxI2CHL
304/303	E11HLxI2CHL
286/285	B3HLxI2CHL
298/297	B10HLxI2CHL

[0277] The aforementioned constructs containing the variable light-chain (L) and variable heavy-chain (H) domains cross-species specific for human and macaque CD33 and the CD3 specific VH and VL combinations cross-species specific for human and macaque CD3 were obtained by gene synthesis. The gene synthesis fragments were designed and eukaryotic protein expression was performed similar as described in example 9 for the MCSP and CD3 cross-species specific single chain molecules. The same holds true for the expression and purification of the CD33 and CD3 cross-species specific single chain molecules.

[0278] In the Western Blot a single band was detected at 52 kD corresponding to the purified bispecific antibody.

16.4. Flow cytometric binding analysis of the CD33 and CD3 cross-species specific bispecific antibodies

[0279] In order to test the functionality of the cross-species specific bispecific antibody constructs regarding the capability to bind to human and macaque CD33 and CD3, respectively, a FACS analysis was performed similar to the analysis described for the analysis of the MCSP and CD3 cross-species specific bispecific antibodies in example 10 using CHO cells expressing the human or macaque CD33 extracellular domains (see example 16.1 and 16.2).

[0280] The specific binding of human and non-chimpanzee primate CD3 of the CD3 binding molecules of the invention was clearly detectable as shown in Figure 29. In the FACS analysis all constructs show binding to CD3 and CD33 as compared to the respective negative controls. Cross-species specificity of the bispecific antibodies to human and macaque CD3 and CD33 antigens is demonstrated.

16.5. Bioactivity of CD33 and CD3 cross-species specific bispecific antibodies

[0281] Bioactivity of the generated bispecific antibodies was analyzed by chromium 51 (⁵¹Cr) release in vitro cytotoxicity

assays using the CD33 positive cell lines described in Examples 16.1 and 16.2. As effector cells stimulated human CD4/CD56 depleted PBMC or the macaque T cell line 4119LnPx were used as specified in the respective figures. The cytotoxicity assays were performed similar to the setting described for the bioactivity analysis of the MCSP and CD3 cross-species specific bispecific antibodies in example 11 using CHO cells expressing the human or macaque CD33 extracellular domains (see example 16.1 and 16.2) as target cells.

[0282] As shown in Figure 30, all of the generated cross-species specific bispecific constructs demonstrate cytotoxic activity against human CD33 positive target cells elicited by stimulated human CD4/CD56 depleted PBMC and against macaque CD33 positive target cells elicited by the macaque T cell line 4119LnPx.

17. Purification of cross-species specific bispecific single chain molecules by an affinity procedure based on the context independent CD3 epsilon epitope corresponding to the N-terminal amino acids 1-27

17.1 Generation of an affinity column displaying the isolated context independent human CD3 epsilon epitope corresponding to the N-terminal amino acids 1-27

[0283] The plasmid for expression of the construct 1-27 CD3-Fc consisting of the 1-27 N-terminal amino acids of the human CD3 epsilon chain fused to the hinge and Fc gamma region of human immunoglobulin IgG1 described above (Example 3; cDNA sequence and amino acid sequence of the recombinant fusion protein are listed under SEQ ID NOs 230 and 229) was transfected into DHFR deficient CHO cells for eukaryotic expression of the construct. Eukaryotic protein expression in DHFR deficient CHO cells was performed as described by Kaufmann R.J. (1990) Methods Enzymol. 185, 537-566. Gene amplification of the construct was induced by increasing concentrations of methotrexate (MTX) to a final concentration of up to 20 nM MTX. After two passages of stationary culture the cells were grown in roller bottles with nucleoside-free HyQ PF CHO liquid soy medium (with 4.0 mM L-Glutamine with 0.1% Pluronic F - 68; HyClone) for 7 days before harvest. The cells were removed by centrifugation and the supernatant containing the expressed protein was stored at -20°C. For the isolation of the fusion protein a goat anti-human fc affinity column was prepared according to standard protocols using a commercially available affinity purified goat anti-human IgG fc fragment specific antibody with minimal cross-reaction to bovine, horse, and mouse serum proteins (Jackson ImmunoResearch Europe Ltd.). Using this affinity column the fusion protein was isolated out of cell culture supernatant on an Akta Explorer System (GE Amersham) and eluted by citric acid. The eluate was neutralized and concentrated. After dialysis against amine free coupling buffer the purified fusion protein was coupled to an N-Hydroxy-Succinimide NHS activated 1 ml HiTrap column (GE Amersham).

[0284] After coupling remaining NHS groups were blocked and the column was washed and stored at 5°C in storage buffer containing 0.1% sodium azide.

17.2 Purification of cross-species specific bispecific single chain molecules using a human CD3 peptide affinity column

[0285] 200 ml cell culture supernatant of cells expressing cross-species specific bispecific single chain molecules were 0.2 µm sterile filtered and applied to the CD3 peptide affinity column using an Akta Explorer system (GE Amersham).

[0286] The column was then washed with phosphate buffered saline PBS pH 7.4 to wash out unbound sample. Elution was done with an acidic buffer pH 3.0 containing 20 mM Citric acid and 1 M sodium chloride. Eluted protein was neutralized immediately by 1 M Trishydroxymethylamine TRIS pH 8.3 contained in the collection tubes of the fraction collector.

[0287] Protein analysis was done by SDS PAGE and Western Blot.

[0288] For SDS PAGE BisTris Gels 4-12% are used (Invitrogen). The running buffer was 1 × MES-SDS-Puffer (Invitrogen). As protein standard 15 µl prestained Sharp Protein Standard (Invitrogen) was applied. Electrophoresis was performed for 60 minutes at 200 volts 120 mA max. Gels were washed in demineralised water and stained with Coomassie for one hour. Gels are destained in demineralised water for 3 hours. Pictures are taken with a Syngene Gel documentation system.

[0289] For Western Blot a double of the SDS PAGE gel was generated and proteins were electroblotted onto a nitrocellulose membrane. The membrane was blocked with 2% bovine serum albumin in PBS and incubated with a biotinylated murine Penta His antibody (Qiagen). As secondary reagent a streptavidin alkaline phosphatase conjugate (DAKO) was used. Blots were developed with BCIP/NBT substrate solution (Pierce).

[0290] As demonstrated in Figures 31, 32 and 33 the use of a human CD3 peptide affinity column as described above allows the highly efficient purification of the bispecific single chain molecules from cell culture supernatant. The cross-species specific anti-CD3 single chain antibodies contained in the bispecific single chain molecules therefore enable via their specific binding properties an efficient generic one-step method of purification for the cross-species specific bispecific single chain molecules, without the need of any tags solely attached for purification purposes.

18. Generic pharmacokinetic assay for cross-species specific bispecific single chain molecules

18.1 Production of 1-27 CD3-Fc for use in the pharmacokinetic assay

[0291] The coding sequence of the 1-27 N-terminal amino acids of the human CD3 epsilon chain fused to the hinge and Fc gamma region of human immunoglobulin IgG1 was obtained by gene synthesis according to standard protocols (cDNA sequence and amino acid sequence of the recombinant fusion protein are listed under SEQ ID NOs 309 and 310). The gene synthesis fragment was designed as to contain first a Kozak site for eukaryotic expression of the construct, followed by a 19 amino acid immunoglobulin leader peptide, followed in frame by the coding sequence of the first 27 amino acids of the extracellular portion of the mature human CD3 epsilon chain, followed in frame by the coding sequence of the hinge region and Fc gamma portion of human IgG1 and a stop codon. The gene synthesis fragment was also designed and cloned as described in example 3.1, supra. A clone with sequence-verified nucleotide sequence was transfected into DHFR deficient CHO cells for eukaryotic expression of the construct. Eukaryotic protein expression in DHFR deficient CHO cells was performed as described in example 9, supra. For the isolation of the fusion protein a goat anti-human fc affinity column was prepared according to standard protocols using a commercially available affinity purified goat anti-human IgG fc fragment specific antibody with minimal cross-reaction to bovine, horse, and mouse serum proteins (Jackson ImmunoResearch Europe Ltd.). Using this affinity column the fusion protein was isolated out of cell culture supernatant on an Äkta Explorer System (GE Amersham) and eluted by citric acid. The eluate was neutralized and concentrated.

18.2 Pharmacokinetic assay for cross-species specific bispecific single chain molecules

[0292] The assay is based on the ECL-ELISA technology using ruthenium labelled detection on carbon plates measured on a Sektor Imager device (MSD). In a first step, carbon plates (MSD High Bind Plate 96 well Cat: L15xB-3) were coated with 5 µl/well at 50 ng/ml of the purified 1-27 CD3-Fc described in Example 18.1. The plate was then dried overnight at 25°C. Subsequently plates were blocked with 5% BSA (Paesel&Lorei #100568) in PBS at 150 µl/well for 1h at 25°C in an incubator while shaking (700 rpm). In the next step plates were washed three times with 0.05% Tween in PBS. A standard curve in 50% macaque serum in PBS was generated by serial 1:4 dilution starting at 100 ng/ml of the respective cross-species specific bispecific single chain molecule to be detected in the assay. Quality control (QC) samples were prepared in 50% macaque serum in PBS ranging from 1 ng/ml to 50 ng/ml of the respective cross-species specific bispecific single chain molecule dependent on the expected sample serum concentrations. Standard, QC or unknown samples were transferred to the carbon plates at 10 µl/well and incubated for 90 min at 25°C in the incubator while shaking (700 rpm). Subsequently plates were washed three times with 0.05% Tween in PBS. For detection 25 µl/well of penta-His-Biotin antibody (Qiagen, 200 µg/ml in 0.05% Tween in PBS) was added and incubated for 1 h at 25°C in an incubator while shaking (700 rpm). In a second detection step 25 µl/well Streptavidin-SulfoTag solution (MSD; Cat: R32AD-1; Lot: W0010903) was added and incubated for 1 h at 25°C in an incubator while shaking (700 rpm). Subsequently plates were washed three times with 0.05% Tween in PBS. Finally 150 µl/well MSD Reading Buffer (MSD, Cat: R9ZC-1) was added and plates were read in the Sektor Imager device.

[0293] Figures 34 and 35 demonstrate the feasibility of detection of cross-species specific bispecific single chain molecules in serum samples of macaque monkeys for cross-species specific bispecific single chain molecules. The cross-species specific anti-CD3 single chain antibodies contained in the bispecific single chain molecules enable therefore via their specific binding properties a highly sensitive generic assay for detection of the cross-species specific bispecific single chain molecules. The assay set out above can be used in the context of formal toxicological studies that are needed for drug development and can be easily adapted for measurement of patient samples in connection with the clinical application of cross-species specific bispecific single chain molecules.

19. Generation of recombinant transmembrane fusion proteins of the N-terminal amino acids 1-27 of CD3 epsilon from different non-chimpanzee primates fused to EpCAM from cynomolgus monkey (1-27 CD3-EpCAM).

19.1 Cloning and expression of 1-27 CD3-EpCAM

[0294] CD3 epsilon was isolated from different non-chimpanzee primates (marmoset, tamarin, squirrel monkey) and swine. The coding sequences of the 1-27 N-terminal amino acids of CD3 epsilon chain of the mature human, common marmoset (*Callithrix jacchus*), cottontop tamarin (*Saguinus oedipus*), common squirrel monkey (*Saimiri sciureus*) and domestic swine (*Sus scrofa*; used as negative control) fused to the N-terminus of Flag tagged cynomolgus EpCAM were obtained by gene synthesis according to standard protocols (cDNA sequence and amino acid sequence of the recombinant fusion proteins are listed under SEQ ID NOs 231 to 240). The gene synthesis fragments were designed as to contain first a BsrGI site to allow for fusion in correct reading frame with the coding sequence of a 19 amino acid

immunoglobulin leader peptide already present in the target expression vector, which was followed in frame by the coding sequence of the N-terminal 1-27 amino acids of the extracellular portion of the mature CD3 epsilon chains, which was followed in frame by the coding sequence of a Flag tag and followed in frame by the coding sequence of the mature cynomolgus EpCAM transmembrane protein. The gene synthesis fragments were also designed to introduce a restriction site at the end of the cDNA coding for the fusion protein. The introduced restriction sites BsrGI at the 5' end and Sall at the 3' end, were utilized in the following cloning procedures. The gene synthesis fragments were then cloned via BsrGI and Sall into a derivative of the plasmid designated pEF-DHFR (pEF-DHFR is described in Raum et al. Cancer Immunol Immunother 50 (2001) 141-150), which already contains the coding sequence of the 19 amino acid immunoglobulin leader peptide following standard protocols. Sequence verified plasmids were used to transfect DHFR deficient CHO cells for eukaryotic expression of the construct. Eukaryotic protein expression in DHFR deficient CHO cells was performed as described by Kaufmann R.J. (1990) Methods Enzymol. 185, 537-566. Gene amplification of the construct was induced by increasing concentrations of methotrexate (MTX) to a final concentration of up to 20 nM MTX.

[0295] Transfectants were tested for cell surface expression of the recombinant transmembrane protein via an FACS assay according to standard protocols. For that purpose a number of 2.5×10^5 cells were incubated with 50 μ l of the anti-Flag M2 antibody (Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany) at 5 μ g/ml in PBS with 2% FCS. Bound antibody was detected with an R-Phycoerythrin-conjugated affinity purified F(ab')₂ fragment, goat anti-mouse IgG, Fc-gamma fragment specific 1:100 in PBS with 2% FCS (Jackson ImmunoResearch Europe Ltd., Newmarket, Suffolk, UK). Flow cytometry was performed on a FACS-Calibur apparatus, the CellQuest software was used to acquire and analyze the data (Becton Dickinson biosciences, Heidelberg). FACS staining and measuring of the fluorescence intensity were performed as described in Current Protocols in Immunology (Coligan, Kruisbeek, Margulies, Shevach and Strober, Wiley-Interscience, 2002).

[0296] Expression of the Flag tagged recombinant transmembrane fusion proteins consisting of cynomolgus EpCAM and the 1-27 N-terminal amino acids of the human, marmoset, tamarin, squirrel monkey and swine CD3 epsilon chain respectively on transfected cells is clearly detectable (Figure 36).

19.2 Cloning and expression of the cross-species specific anti-CD3 single chain antibody I2C HL in form of an IgG1 antibody

[0297] In order to provide improved means of detection of binding of the cross-species specific single chain anti-CD3 antibody the I2C VHVL specificity is converted into an IgG1 antibody with murine IgG1 and murine kappa constant regions. cDNA sequences coding for the heavy chain of the IgG antibody were obtained by gene synthesis according to standard protocols. The gene synthesis fragments were designed as to contain first a Kozak site to allow for eukaryotic expression of the construct, which is followed by an 19 amino acid immunoglobulin leader peptide, which is followed in frame by the coding sequence of the heavy chain variable region or light chain variable region, followed in frame by the coding sequence of the heavy chain constant region of murine IgG1 as published in GenBank (Accession number AB097849) or the coding sequence of the murine kappa light chain constant region as published in GenBank (Accession number D14630), respectively.

[0298] Restriction sites were introduced at the beginning and the end of the cDNA coding for the fusion protein. Restriction sites EcoRI at the 5' end and Sall at the 3' end were used for the following cloning procedures. The gene synthesis fragments were cloned via EcoRI and Sall into a plasmid designated pEF-DHFR (pEF-DHFR is described in Raum et al. Cancer Immunol Immunother 50 (2001) 141-150) for the heavy chain construct and pEFADA (pEFADA is described in Raum et al. loc cit.) for the light chain construct according to standard protocols. Sequence verified plasmids were used for co-transfection of respective light and heavy chain constructs into DHFR deficient CHO cells for eukaryotic expression of the construct. Eukaryotic protein expression in DHFR deficient CHO cells was performed as described by Kaufmann R.J. (1990) Methods Enzymol. 185, 537-566. Gene amplification of the constructs was induced by increasing concentrations of methotrexate (MTX) to a final concentration of up to 20 nM MTX and deoxycoformycin (dCF) to a final concentration of up to 300 nM dCF. After two passages of stationary culture cell culture supernatant was collected and used in the subsequent experiment.

19.3 Binding of the cross-species specific anti-CD3 single chain antibody I2C HL in form of an IgG1 antibody to 1-27 CD3-EpCAM

[0299] Binding of the generated I2C IgG1 construct to the 1-27 N-terminal amino acids of the human, marmoset, tamarin and squirrel monkey CD3 epsilon chains respectively fused to cynomolgus Ep-CAM as described in Example 19.1 was tested in a FACS assay according to standard protocols. For that purpose a number of 2.5×10^5 cells were incubated with 50 μ l of cell culture supernatant containing the I2C IgG1 construct as described in Example 19.2. The binding of the antibody was detected with an R-Phycoerythrin-conjugated affinity purified F(ab')₂ fragment, goat anti-mouse IgG, Fc-gamma fragment specific, diluted 1:100 in PBS with 2% FCS (Jackson ImmunoResearch Europe Ltd.,

Newmarket, Suffolk, UK). Flow cytometry was performed on a FACS-Calibur apparatus, the CellQuest software was used to acquire and analyze the data (Becton Dickinson biosciences, Heidelberg). FACS staining and measuring of the fluorescence intensity were performed as described in Current Protocols in Immunology (Coligan, Kruisbeek, Margulies, Shevach and Strober, Wiley-Interscience, 2002).

[0300] As shown in Figure 37 binding of the I2C IgG1 construct to the transfectants expressing the recombinant transmembrane fusion proteins consisting of the 1-27 N-terminal amino acids of CD3 epsilon of human, marmoset, tamarin or squirrel monkey fused to cynomolgus EpCAM as compared to the negative control consisting of the 1-27 N-terminal amino acids of CD3 epsilon of swine fused to cynomolgus EpCAM was observed. Thus multi-primate cross-species specificity of I2C was demonstrated. Signals obtained with the anti Flag M2 antibody and the I2C IgG1 construct were comparable, indicating a strong binding activity of the cross-species specific specificity I2C to the N-terminal amino acids 1-27 of CD3 epsilon.

20. Binding of the cross-species specific anti-CD3 binding molecule I2C to the human CD3 epsilon chain with and without N-terminal His6 tag

[0301] A chimeric IgG1 antibody with the binding specificity I2C as described in Example 19.2 specific for CD3 epsilon was tested for binding to human CD3 epsilon with and without N-terminal His6 tag. Binding of the antibody to the EL4 cell lines transfected with His6-human CD3 epsilon as described in Example 6.1 and wild-type human CD3 epsilon as described in Example 5.1 respectively was tested by a FACS assay according to standard protocols. 2.5×10^5 cells of the transfectants were incubated with 50 μ l of cell culture supernatant containing the I2C IgG1 construct or 50 μ l of the respective control antibodies at 5 μ g/ml in PBS with 2% FCS. As negative control an appropriate isotype control and as positive control for expression of the constructs the CD3 specific antibody UCHT-1 were used respectively. Detection of the His6 tag was performed with the penta His antibody (Qiagen). The binding of the antibodies was detected with a R-Phycoerythrin-conjugated affinity purified F(ab')₂ fragment, goat anti-mouse IgG, Fc-gamma fragment specific, diluted 1:100 in PBS with 2% FCS (Jackson ImmunoResearch Europe Ltd., Newmarket, Suffolk, UK). Flow cytometry was performed on a FACS-Calibur apparatus, the CellQuest software was used to acquire and analyze the data (Becton Dickinson biosciences, Heidelberg). FACS staining and measuring of the fluorescence intensity were performed as described in Current Protocols in Immunology (Coligan, Kruisbeek, Margulies, Shevach and Strober, Wiley-Interscience, 2002).

[0302] Comparable binding of the anti-human CD3 antibody UCHT-1 to both transfectants demonstrates approximately equal levels of expression of the constructs. The binding of the penta His antibody confirmed the presence of the His6 tag on the His6-human CD3 construct but not on the wild-type construct.

[0303] Compared to the EL4 cell line transfected with wild-type human CD3 epsilon a clear loss of binding of the I2C IgG1 construct to human-CD3 epsilon with an N-terminal His6 tag was detected. These results show that a free N-terminus of CD3 epsilon is essential for binding of the cross-species specific anti-CD3 binding specificity I2C to the human CD3 epsilon chain (Figure 28).

21. Generation of CD33 and CD3 cross-species specific bispecific single chain molecules

21.1 Generation of CD33 and CD3 cross-species specific bispecific single chain molecules

[0304] Generally, bispecific single chain antibody molecules, each comprising a domain with a binding specificity cross-species specific for human and macaque CD3epsilon as well as a domain with a binding specificity cross-species specific for human and macaque CD33, were designed as set out in the following Table 6:

Table 6: Formats of anti-CD3 and anti-CD33 cross-species specific bispecific single chain antibody molecules

SEQ ID (nucl/prot)	Formats of protein constructs (N -> C)
316/315	I2CHLxAF5HL
314/313	F12QHLxAF5HL
312/311	H2CHLxAF5HL

[0305] The aforementioned constructs containing the variable light-chain (L) and variable heavy-chain (H) domains cross-species specific for human and macaque CD33 and the CD3 specific VH and VL combinations cross-species specific for human and macaque CD3 were obtained by gene synthesis. The gene synthesis fragments were designed in analogy to the procedure described in example 9 for the MCSP and CD3 cross-species specific single chain molecules.

A clone with sequence-verified nucleotide sequence was transfected into DHFR deficient CHO cells for eukaryotic expression of the construct. Eukaryotic protein expression in DHFR deficient CHO cells was performed as also described in example 9 for the MCSP and CD3 cross-species specific single chain molecules and used in the subsequent experiments.

21.2 Flow cytometric binding analysis of the CD33 and CD3 cross-species specific bispecific antibodies

[0306] In order to test the functionality of the cross-species specific bispecific antibody constructs regarding the capability to bind to human and macaque CD33 and CD3, respectively, a FACS analysis is performed similar to the analysis described for the analysis of the MCSP and CD3 cross-species specific bispecific antibodies in example 10 using CHO cells expressing the human or macaque CD33 extracellular domains (see examples 16.1 and 16.2).

[0307] The bispecific binding of the single chain molecules listed above, which were cross-species specific for CD33 and cross-species specific for human and non-chimpanzee primate CD3 was clearly detectable as shown in Figure 41. In the FACS analysis all constructs showed binding to CD3 and CD33 as compared to the respective negative controls. Cross-species specificity of the bispecific antibodies to human and macaque CD3 and CD33 antigens was demonstrated.

21.3. Bioactivity of CD33 and CD3 cross-species specific bispecific single chain antibodies

[0308] Bioactivity of the generated bispecific single chain antibodies was analyzed by chromium 51 (⁵¹Cr) release in vitro cytotoxicity assays using the CD33 positive cell lines described in Examples 16.1 and 16.2. As effector cells stimulated human CD4/CD56 depleted PBMC or the macaque T cell line 4119LnPx were used as specified in the respective figures. The cytotoxicity assays were performed similar to the procedure described for the bioactivity analysis of the MCSP and CD3 cross-species specific bispecific antibodies in example 11 using CHO cells expressing the human or macaque CD33 extracellular domains (see example 16.1 and 16.2) as target cells.

[0309] As shown in Figure 42, all of the generated cross-species specific bispecific single chain antibody constructs demonstrate cytotoxic activity against human CD33 positive target cells elicited by stimulated human CD4/CD56 depleted PBMC and against macaque CD33 positive target cells elicited by the macaque T cell line 4119LnPx.

22. Redistribution of circulating chimpanzee T cells upon exposure to a conventional bispecific CD3 binding molecule directed at a target molecule which is absent from circulating blood cells

[0310] A single male chimpanzee was subjected to dose escalation with intravenous single-chain EpCAM/CD3-bispecific antibody construct (Schlereth (2005) Cancer Res 65: 2882). Like in the conventional single-chain CD19/CD3-bispecific antibody construct (Loffler (2000, Blood, Volume 95, Number 6) or WO 99/54440), the CD3 arm of said EpCAM/CD3-construct is also directed against a conventional context dependent epitope of human and chimpanzee CD3. At day 0, the animal received 50ml PBS/5% HSA without test material, followed by 50ml PBS/5% HSA plus single-chain EpCAM/CD3-bispecific antibody construct at 1.6, 2.0, 3.0 and 4.5 µg/kg on days 7, 14, 21 and 28, respectively. The infusion period was 2 hours per administration. For each weekly infusion the chimpanzee was sedated with 2-3 mg/kg Telazol intramuscularly, intubated and placed on isoflurane/O₂ anesthesia with stable mean blood pressures. A second intravenous catheter was placed in an opposite limb to collect (heparinized) whole blood samples at the time points indicated in Figure 43 for FACS analysis of circulating blood cells. After standard erythrocyte lysis, T cells were stained with a FITC-labeled antibody reacting with chimpanzee CD2 (Becton Dickinson) and the percentage of T cells per total lymphocytes determined by flowcytometry. As shown in Figure 43, every administration of single-chain EpCAM/CD3-bispecific antibody construct induced a rapid drop of circulating T cells as observed with single-chain CD19/CD3-bispecific antibody construct in B-NHL patients, who had essentially no circulating target B (lymphoma) cells. As there are no EpCAM-positive target cells in the circulating blood of humans and chimpanzees, the drop of circulating T cells upon exposure to the single-chain EpCAM/CD3-bispecific antibody construct can be attributed solely to a signal, which the T cells receive through pure interaction of the CD3 arm of the construct with a conventional context dependent CD3 epitope in the absence of any target cell mediated crosslinking. Like the redistribution of T cells induced through their exposure to single-chain CD19/CD3-bispecific antibody construct in B-NHL patients, who had essentially no circulating target B (lymphoma) cells, the T cell redistribution in the chimpanzee upon exposure to the single-chain EpCAM/CD3-bispecific antibody construct can be explained by a conformational change of CD3 following the binding event to a context dependent CD3 epitope further resulting in the transient increase of T cell adhesiveness to blood vessel endothelium (see Example 13). This finding confirms, that conventional CD3 binding molecules directed to context dependent CD3 epitopes - solely through this interaction - can lead to a redistribution pattern of peripheral blood T cells, which is associated with the risk of CNS adverse events in humans as describe in Example 13.

23. Specific binding of scFv clones to the N-terminus of human CD3 epsilon

23.1 Bacterial expression of scFv constructs in *E. coli* XL1 Blue

[0311] As previously mentioned, *E. coli* XL1 Blue transformed with pComb3H5Bhis/Flag containing a VL- and VH-segment produce soluble scFv in sufficient amounts after excision of the gene III fragment and induction with 1 mM IPTG. The scFv-chain is exported into the periplasma where it folds into a functional conformation.

[0312] The following scFv clones were chosen for this experiment:

- i) ScFvs 4-10, 3-106, 3-114, 3-148, 4-48, 3-190 and 3-271 as described in WO 2004/106380.
- ii) ScFvs from the human anti-CD3epsilon binding clones H2C, F12Q and I2C as described herein.

[0313] For periplasmic preparations, bacterial cells transformed with the respective scFv containing plasmids allowing for periplasmic expression were grown in SB-medium supplemented with 20 mM MgCl₂ and carbenicillin 50 µg/ml and redissolved in PBS after harvesting. By four rounds of freezing at -70°C and thawing at 37°C, the outer membrane of the bacteria was destroyed by osmotic shock and the soluble periplasmic proteins including the scFvs were released into the supernatant. After elimination of intact cells and cell-debris by centrifugation, the supernatant containing the human anti-human CD3-scFvs was collected and used for further examination. These crude supernatants containing scFv will be further termed periplasmic preparations (PPP).

23.2 Binding of scFvs to human CD3 epsilon (aa 1-27)-Fc fusion protein

[0314] ELISA experiments were carried out by coating the human CD3 epsilon (aa 1-27)-Fc fusion protein to the wells of 96 well plastic plates (Nunc, maxisorb) typically at 4° C over night. The antigen coating solution was then removed, wells washed once with PBS/0.05 % Tween 20 and subsequently blocked with PBS/3 % BSA for at least one hour. After removal of the blocking solution, PPPs and control solutions were added to the wells and incubated for typically one hour at room temperature. The wells were then washed three times with PBS/0.05 % Tween 20. Detection of scFvs bound to immobilized antigen was carried out using a Biotin-labeled anti FLAG-tag antibody (M2 anti Flag-Bio, Sigma, typically at a final concentration of 1 µg/ml PBS) and detected with a peroxidase-labeled Streptavidine (Dianova, 1 µg/ml PBS). The signal was developed by adding ABTS substrate solution and measured at a wavelength of 405 nm. Unspecific binding of the test-samples to the blocking agent and/or the human IgG1 portion of the human CD3 epsilon (aa 1-27)-Fc fusion protein was examined by carrying out the identical assay with the identical reagents and identical timing on ELISA plates which were coated with human IgG1 (Sigma). PBS was used as a negative control.

[0315] As shown in Figure 44, scFvs H2C, F12Q and I2C show strong binding signals on human CD3 epsilon (aa 1-27)-Fc fusion protein. The human scFvs 3-106, 3-114, 3-148, 3-190, 3-271, 4-10 and 4-48 (as described in WO 2004/106380) do not show any significant binding above negative control level.

[0316] To exclude the possibility that the positive binding of scFvs H2C, F12Q and I2C to wells coated with human CD3 epsilon (aa 1-27)-Fc fusion protein might be due to binding to BSA (used as a blocking agent) and/or the human IgG1 Fc-gamma-portion of the human CD3 epsilon (aa 1-27)-Fc fusion protein, a second ELISA experiment was performed in parallel. In this second ELISA experiment, all parameters were identical to those in the first ELISA experiment, except that in the second ELISA experiment human IgG1 (Sigma) was coated instead of human CD3 epsilon (aa 1-27)-Fc fusion protein. As shown in Figure 45, none of the scFvs tested showed any significant binding to BSA and/or human IgG1 above background level.

[0317] Taken together, these results allow the conclusion that conventional CD3 binding molecules recognizing a context-dependent epitope of CD3 epsilon (e.g. as disclosed in WO 2004/106380) do not bind specifically to the human CD3 epsilon (aa 1-27)-region, whereas the scFvs H2C, F12Q and I2C binding a context-independent epitope of CD3 epsilon clearly show specific binding to the N-terminal 27 amino acids of human CD3 epsilon.

24. Generation and characterization of PSMA and CD3 cross-species specific bispecific single chain antibody molecules

24.1 Cloning and expression of human PSMA antigen on CHO cells

[0318] The sequence of the human PSMA antigen ('AY101595', Homo sapiens prostate-specific membrane antigen mRNA, complete cds, National Center for Biotechnology Information, <http://www.ncbi.nlm.nih.gov/entrez>) was used to obtain a synthetic molecule by gene synthesis according to standard protocols. The gene synthesis fragment was also designed as to contain a Kozak site for eukaryotic expression of the construct and restriction sites at the beginning and the end of the DNA. The introduced restriction sites XbaI at the 5' end and Sall at the 3' end were utilised during the

cloning step into the expression plasmid designated pEFDHFR as described in Mack et al. (Mack M et al., Proc Natl Acad Sci U S A 1995;92:7021-5. and Raum et al. Cancer Immunol Immunother (2001) 50(3)). After sequence verification the plasmid was used to transfect CHO/dhfr- cells as follows. A sequence verified plasmid was used to transfect CHO/dhfr-cells (ATCC No. CRL 9096; cultivated in RPMI 1640 with stabilized glutamine obtained from Biochrom AG Berlin, Germany, supplemented with 10% FCS, 1% penicillin/streptomycin all obtained from Biochrom AG Berlin, Germany and nucleosides from a stock solution of cell culture grade reagents obtained from Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany, to a final concentration of 10 µg/ml Adenosine, 10 µg/ml Deoxyadenosine and 10 µg/ml Thymidine, in an incubator at 37 °C, 95% humidity and 7% CO₂). Transfection was performed using the PolyFect Transfection Reagent (Qiagen GmbH, Hilden, Germany) and 5 µg of plasmid DNA according to the manufacturer's protocol. After a cultivation of 24 hours cells were washed once with PBS and again cultivated in the aforementioned cell culture medium except that the medium was not supplemented with nucleosides and dialysed FCS (obtained from Biochrom AG Berlin, Germany) was used. Thus the cell culture medium did not contain nucleosides and thereby selection was applied on the transfected cells. Approximately 14 days after transfection the outgrowth of resistant cells was observed. After an additional 7 to 14 days the transfectants were tested positive for expression of the construct via FACS. Eukaryotic protein expression in DHFR deficient CHO cells is performed as described by Kaufmann R.J. (1990) Methods Enzymol. 185, 537-566. Gene amplification of the construct is induced by increasing concentrations of methothrexate (MTX) to a final concentration of up to 20 nM MTX

24.2 Cloning and expression of macaque PSMA antigen on CHO cells

[0319] The cDNA sequence of macaque PSMA (cynomolgus) was obtained by a set of five PCRs on cDNA from macaque monkey prostate prepared according to standard protocols. The following reaction conditions: 1 cycle at 94°C for 2 minutes followed by 40 cycles with 94°C for 1 minute, 52°C for 1 minute and 72°C for 1.5 minutes followed by a terminal cycle of 72°C for 3 minutes and the following primers were used:

4. forward primer: 5'-cactgtgcccaggttcgagg-3' (SEQ ID NO. 375)
reverse primer: 5'-gacataccacacaaattcaatacgg-3' (SEQ ID NO. 376)
5. forward primer: 5'-gctctgctcgccgagatgtgg-3' (SEQ ID NO. 377)
reverse primer: 5'-acgctggacaccacctccagg-3' (SEQ ID NO. 378)
6. forward primer: 5'-ggttctactgagtgaggcagagg-3' (SEQ ID NO. 379)
reverse primer: 5'-actgtgtgtgctgcttgaggc-3' (SEQ ID NO. 380)
7. forward primer: 5'-gggtgaagtcctatccagatgg-3' (SEQ ID NO. 381)
reverse primer: 5'-gtgctctgctgaagcaattcc-3' (SEQ ID NO. 382)
8. forward primer: 5'-ctcggcttctctcggtgg-3' (SEQ ID NO. 383)
reverse primer: 5'-gcatattcattgtgggtaacctgg-3' (SEQ ID NO. 384)

[0320] These PCRs generated five overlapping fragments, which were isolated and sequenced according to standard protocols using the PCR primers, and thereby provided a portion of the cDNA sequence coding macaque PSMA from codon 3 to the last codon of the mature protein. To generate a construct for expression of macaque PSMA a cDNA fragment was obtained by gene synthesis according to standard protocols (the cDNA and amino acid sequence of the construct is listed under SEQ ID 385 and 386). In this construct the coding sequence of macaque PSMA from amino acid 3 to the last amino acid of the mature PSMA protein followed by a stop codon was fused in frame to the coding sequence of the first two amino acids of the human PSMA protein. The gene synthesis fragment was also designed as to contain a Kozak site for eukaryotic expression of the construct and restriction sites at the beginning and the end of the fragment containing the cDNA. The introduced restriction sites, XbaI at the 5' end and Sall at the 3' end, were utilised in the following cloning procedures. The gene synthesis fragment was cloned via XbaI and Sall into a plasmid designated pEF-DHFR following standard protocols. The aforementioned procedures were carried out according to standard protocols (Sambrook, Molecular Cloning; A Laboratory Manual, 3rd edition, Cold Spring Harbour Laboratory Press, Cold Spring Harbour, New York (2001)). A clone with sequence-verified nucleotide sequence was transfected into DHFR deficient CHO cells for eukaryotic expression of the construct. Eukaryotic protein expression in DHFR deficient CHO cells was performed as described by Kaufmann R.J. (1990) Methods Enzymol. 185, 537-566. Gene amplification of the construct was induced by increasing concentrations of methotrexate (MTX) to a final concentration of up to 20 nM MTX.

24.3 Generation of PSMA and CD3 cross-species specific bispecific single chain molecules

[0321] Generally, bispecific single chain antibody molecules, each comprising a domain with a binding specificity for the human and the macaque CD3 antigen as well as a domain with a binding specificity for the human and the macaque PSMA antigen, were designed as set out in the following Table 7:

Table 7: Formats of anti-CD3 and anti-PSMA cross-species specific bispecific single chain antibody molecules

SEQ ID NO. (nucl/prot)	Formats of protein constructs (N → C)
400/399	PSMA-3 HL × I2C HL
414/413	PSMA-4 HL × I2C HL
428/427	PSMA-6 LH × I2C HL
442/441	PSMA-7 LH × I2C HL
456/455	PSMA-8 LH × I2C HL
470/469	PSMA-9 LH × I2C HL
484/483	PSMA-10 LH × I2C HL
498/497	PSMA-A LH × I2C HL
512/511	PSMA-B LH × I2C HL
526/525	PSMA-C LH × I2C HL
540/539	PSMA-D LH × I2C HL
554/553	PSMA-E LH × I2C HL
568/567	PSMA-F LH × I2C HL
582/581	PSMA-J LH × I2C HL
596/595	PSMA-L LH × I2C HL

[0322] The aforementioned constructs containing the variable light-chain (L) and variable heavy-chain (H) domains cross-species specific for human and macaque PSMA and the CD3 specific VH and VL combinations cross-species specific for human and macaque CD3 were obtained by gene synthesis. The gene synthesis fragments were designed and eukaryotic protein expression was performed in analogy to the procedure described in example 9 for the MCSP and CD3 cross-species specific single chain molecules. Alternatively the constructs can be transfected into DHFR-deficient CHO-cells in a transient manner according to standard protocols.

24.4 Flow cytometric binding analysis of the PSMA and CD3 cross-species specific bispecific antibodies

[0323] In order to test the functionality of the cross-species specific bispecific antibody constructs with regard to binding capability to human and macaque PSMA and to human and macaque CD3, a FACS analysis was performed. For this purpose the CHO cells transfected with human PSMA as described in Example 24.1 and human CD3 positive T cell leukemia cell line HPB-ALL (DSMZ, Braunschweig, ACC483) were used to check the binding to human antigens. The binding reactivity to macaque antigens was tested by using the generated macaque PSMA transfectant described in Example 24.2 and a macaque T cell line 4119LnPx (kindly provided by Prof Fickenscher, Hygiene Institute, Virology, Erlangen-Nuernberg; published in Knappe A, et al., and Fickenscher H., Blood 2000, 95, 3256-61). The flow cytometric analysis was performed in analogy to the procedure described in example 10.

[0324] The binding ability of all PSMA based bispecific single chain molecules were clearly detectable as shown in Figure 46. In the FACS analysis, all constructs showed binding to CD3 and PSMA compared to the negative control using culture medium and 1. and 2. detection antibody. In summary, the cross-species specificity of the bispecific antibody to human and macaque CD3 and to human and macaque PSMA could clearly be demonstrated.

24.5 Bioactivity of PSMA and CD3 cross-species specific bispecific single chain antibodies

[0325] Bioactivity of the generated bispecific single chain antibodies was analyzed by chromium 51 release in vitro cytotoxicity assays using the PSMA positive cell lines described in example 24.1 and 24.2. As effector cells stimulated human CD8 positive T cells or the macaque T cell line 4119LnPx were used. The cytotoxicity assays were performed similar to the procedure described for the bioactivity analysis of the MCSP and CD3 cross-species specific bispecific antibodies in example 11.

[0326] As shown in Figures 47 and 48, all of the depicted cross-species specific bispecific single chain antibody constructs revealed cytotoxic activity against human PSMA positive target cells elicited by human CD8+ cells and against

macaque PSMA positive target cells elicited by the macaque T cell line 4119LnPx. As a negative control, an irrelevant bispecific single chain antibody was used.

24.6 Generation of PSMA and CD3 cross-species specific bispecific single chain molecules

[0327] Bispecific single chain antibody molecules, each comprising a domain binding to the human and to the macaque CD3 antigen as well as a domain binding to the human PSMA antigen, were designed as set out in the following Table 8:

Table 8: Formats of anti-CD3 and anti-PSMA cross-species specific bispecific single chain antibody molecules

SEQ ID NO. (nucl/prot)	Formats of protein constructs (N → C)
610/609	PM99-A8 HL x I2C HL
624/623	PM86-A10 HL x I2C HL
638/637	PM86-B4-2 HL x I2C HL
652/651	PM98-B4 HL x I2C HL
666/665	PM86-C3 HL x I2C HL
680/679	PM86-E12 HL x I2C HL
694/693	PMF1-A10 HL x I2C HL
708/707	PM99-F1 HL x I2C HL
736/721	PM99-F5 HL x I2C HL
735/734	PM86-F6 HL x I2C HL
800/799	PM76-A9 HL x I2C HL
818/817	PM76-B10 HL x I2C HL
864/863	PM29-G1 HL x I2C HL
850/849	PM49-B9 HL x I2C HL
836/835	PM34-C7 HL x I2C HL
786/785	PM84-D7 HL x I2C HL
882/881	PM08-B6 HL x I2C HL
900/899	PM08-E11 HL x I2C HL
936/935	PM95-A8 HL x I2C HL
1018/1017	PM26-C9 HL x I2C HL
1032/1031	PM26-H4 HL x I2C HL
918/917	PM95-H6 HL x I2C HL
1004/1003	PM07-D3 HL x I2C HL
954/953	PM07-A12 HL x I2C HL
972/971	PM07-F8 HL x I2C HL
990/989	PM07-E5 HL x I2C HL

[0328] The aforementioned constructs each comprising a combination of a variable light-chain (L) and a variable heavy-chain (H) domain binding to the human and to the macaque CD3 antigen as well as a combination of a variable light-chain (L) and a variable heavy-chain (H) domains binding to the human PSMA antigen were obtained by gene synthesis. Each combination of a variable light-chain (L) and a variable heavy-chain (H) domains binding to the human PSMA antigen was obtained via phage display from a scFv-library by panning on the PSMA-positive human prostate cancer cell line LNCaP (ATCC No. CRL-1740) followed by FACS-based screening for positive clones using the same cell line. The gene synthesis fragments of the above listed bispecific single chain antibody molecules were designed and eukaryotic protein expression was performed in analogy to the procedure described in example 24.3, supra, re-

spectively for the MCSP and CD3 cross-species specific single chain molecules in example 9. The same holds true for the expression and purification of the PSMA and CD3 bispecific single chain antibody molecules.

24.7 Flow cytometric binding analysis of PSMA and CD3 cross-species specific bispecific antibodies

[0329] In order to test the functionality of cross-species specific bispecific antibody constructs regarding the capability to bind to PSMA and CD3 a FACS analysis was performed. For this purpose PSMA-positive cells were used to test the binding to human antigens. The binding reactivity to macaque CD3 was tested by using the macaque T cell line 4119LnPx (kindly provided by Prof Fickenscher, Hygiene Institute, Virology, Erlangen-Nuernberg; published in Knappe A, et al., and Fickenscher H., Blood 2000, 95, 3256-61). The flow cytometric analysis was performed in analogy to the procedure described in example 10.

[0330] The bispecific binding of the generated single chain molecules shown in Figure 49 and Figure 51, to human PSMA and to human and non-chimpanzee primate CD3 was clearly detectable. In the FACS analysis all shown constructs demonstrated binding to CD3 and PSMA compared to the negative control.

24.8 Bioactivity of PSMA and CD3 cross-species specific bispecific single chain antibodies

[0331] Bioactivity of generated bispecific single chain antibodies was analyzed by chromium 51 (⁵¹Cr) release in vitro cytotoxicity assays using PSMA positive cell lines. As effector cells stimulated human CD4/CD56 depleted PBMC or the macaque T cell line 4119LnPx were used. The cytotoxicity assays were performed similar to the procedure described for the bioactivity analysis of the MCSP and CD3 cross-species specific bispecific antibodies in example 11.

[0332] The generated cross-species specific bispecific single chain antibody constructs shown in Figure 50 and 52 demonstrated cytotoxic activity against PSMA positive target cells.

24.9. Generation of additional PSMA and CD3 cross-species specific bispecific single chain molecules

[0333] The human antibody germline VH sequence VH3 3-11 (<http://vbase.mrc-cpe.cam.ac.uk/>) is chosen as framework context for CDRH1 (SEQ ID NO. 394), CDRH2 (SEQ ID NO. 395) and CDRH3 (SEQ ID NO. 396). Likewise the human antibody germline VH sequence VH1 1-02 (<http://vbase.mrc-cpe.cam.ac.uk/>) is chosen as framework context for CDRH1 (SEQ ID NO. 408), CDRH2 (SEQ ID NO. 409) and CDRH3 (SEQ ID NO. 410) as well as the human antibody germline VH sequence VH1 1-03 (<http://vbase.mrc-cpe.cam.ac.uk/>) as framework context for CDRH1 (SEQ ID NO. 445), CDRH2 (SEQ ID NO. 446) and CDRH3 (SEQ ID NO. 447). For each human VH several degenerated oligonucleotides have to be synthesized that overlap in a terminal stretch of approximately 15-20 nucleotides. To this end every second primer is an antisense primer. For VH3 3-11 the following set of oligonucleotides is used:

5'PM3-VH-A-XhoI

CCG GAT CTC GAG TCT GGC GGC GGA CTG GTG AAG CCT GGC GRG TCC
CTG ARG CTG TCC TGT (SEQ ID NO. 737)

3'PM3-VH-B

CCA GTA CAT GTA GTA GTC GGA GAA GGT GAA GCC GGA GGC GRY ACA
GGA CAG CYT CAG GGA (SEQ ID NO. 738)

5'PM3-VH-C

TAC TAC ATG TAC TGG RTC CGC CAG RCC CCT GRG AAG SGG CTG GAA
TGG GTG KCC ATC ATC TCC GAC GGC (SEQ ID NO. 739)

3'PM3-VH-D

GGC GTT GTC CCG GGA GAT GGT GAA CCG GCC CTT GAT GAT GTC GGA
GTA GTA GGT GTA GTA GCC GCC GTC GGA GAT GAT (SEQ ID NO. 740)

5'PM3-VH-E

TCC CGG GAC AAC GCC AAG AAC ARC CTG TAC CTG CAG ATG ARC TCC
CTG ARG KCC GAG GAC ACC GCC RTG TAC TAC TGC RCC CGG GGC (SEQ ID
NO. 741)

3'PM3-VH-F-BstEII

CGA TAC GGT GAC CAG GGT GCC CTG GCC CCA GTA ATC CAT GGC GCC
GTG TCT CAG CAG AGG GAA GCC CCG GGY GCA GTA GTA (SEQ ID NO. 742)

[0334] For VH1 1-02 the oligonucleotides are as follows:

5'PM4-VH-A-XhoI

CTT GAT CTC GAG TCT GGC GCC GAA STG RWG RAG CCT GGC GCC TCC
GTG AAG STG TCC TGC AAG GCC TCC GGC TAC (SEQ ID NO. 743)

3'PM4-VH-B

CCA TTC CAG GCC CTG CYC AGG CSY CTG CCG CAS CCA GTT GAT GTC
GAA GTA GGT GAA GGT GTA GCC GGA GGC CTT (SEQ ID NO. 744)

5'PM4-VH-C

CAG GGC CTG GAA TGG ATS GGC GGC ATC TCC CCT GGC GAC GGC AAC
ACC AAC TAC AAC GAG AAC TTC AAG (SEQ ID NO. 745)

3'PM4-VH-D

AT GTA GGC GGT GGA GMT GGA CKT GTC TMT GGT CAK TGT GRC CYT GCC
CTT GAA GTT CTC GTT GTA (SEQ ID NO. 746)

5'PM4-VH-E

C TCC ACC GCC TAC ATS SAG CTG TCC CGG CTG ASA TCT GAS GAC ACC
GCC GTG TAC TWC TGC GCC AGG GAC GGC (SEQ ID NO. 747)

3'PM4-VH-F-BstEII

AGA CAC GGT CAC CGT GGT GCC CTG GCC CCA AGA GTC CAT GGC GTA
GTA AGG GAA GTT GCC GTC CCT GGC GCA (SEQ ID NO. 748)

[0335] For VH1 1-03 the following oligonucleotides are used:

5'PM8-VH-A-XhoI

CTT GAT CTC GAG TCC GGC SCT GAG STG RWG AAG CCT GGC GCC TCC
GTG AAG RTG TCC TGC AAG GCC TCC GGC TAC (SEQ ID NO. 749)

3'PM8-VH-B

CCA TTC CAG CMS CTG GCC GGG TKY CTG TYT CAC CCA GTG CAT CAC GTA
GCC GGT GAA GGT GTA GCC GGA GGC CTT GCA (SEQ ID NO. 750)

5'PM8-VH-C

CCC GGC CAG SKG CTG GAA TGG ATS GGC TAC ATC AAC CCT TAC AAC
GAC GTG ACC CGG TAC AAC GGC AAG TTC AAG (SEQ ID NO. 751)

3'PM8-VH-D

TTC CAT GTA GGC GGT GGA GGM GKA CKT GTC KCT GGT AAK GGT GRC
TYT GCC CTT GAA CTT GCC GTT GTA (SEQ ID NO. 752)

5'PM8-VH-E

TCC ACC GCC TAC ATG GAA CTG TCC RGC CTG ASG TCT GAG GAC ACC
GCC GTG TAC TAC TGC GCC AGG GGC (SEQ ID NO. 753)

3'PM8-VH-F-BstEII

CGA TAC GGT GAC CAG AGT GCC TCT GCC CCA GGA GTC GAA GTA GTA
CCA GTT CTC GCC CCT GGC GCA GTA GTA (SEQ ID NO. 754)

[0336] Each of these primer-sets spans over the whole corresponding VH sequence.

[0337] Within each set primers are mixed in equal amounts (e.g. 1 μ l of each primer (primer stocks 20 to 100 μ M) to a 20 μ l PCR reaction) and added to a PCR mix consisting of PCR buffer, nucleotides and Taq polymerase. This mix is incubated at 94 °C for 3 minutes, 65 °C for 1 minute, 62°C for 1 minute, 59 °C for 1 minute, 56 °C for 1 minute, 52 °C for 1 minute, 50 °C for 1 minute and at 72°C for 10 minutes in a PCR cyclor. Subsequently the product is run in an agarose gel electrophoresis and the product of a size from 200 to 400 isolated from the gel according to standard methods.

[0338] Each VH PCR product is then used as a template for a standard PCR reaction using primers that incorporate N-terminal and C-terminal suitable cloning restriction sites. The DNA fragment of the correct size (for a VH approximately 350 nucleotides) is isolated by agarose gel electrophoresis according to standard methods. In this way sufficient VH DNA fragment is amplified.

[0339] The human antibody germline VL sequence Vkl L1 (<http://vbase.mrc-cpe.cam.ac.uk/>) is chosen as framework context for CDRL1 (SEQ ID NO. 389), CDRL2 (SEQ ID NO. 390) and CDRL3 (SEQ ID NO. 391). Likewise human antibody germline VL sequence Vkl A17 (<http://vbase.mrc-cpe.cam.ac.uk/>) is chosen as framework context for CDRL1 (SEQ ID NO. 403), CDRL2 (SEQ ID NO. 404) and CDRL3 (SEQ ID NO. 405) as well as the human antibody germline VL sequence Vkl A1 (<http://vbase.mrc-cpe.cam.ac.uk/>) as framework context for CDRL1 (SEQ ID NO. 450), CDRL2 (SEQ ID NO. 451) and CDRL3 (SEQ ID NO. 452). For each human VL several degenerated oligonucleotides have to be synthesized that overlap in a terminal stretch of approximately 15-20 nucleotides. To this end every second primer is an antisense primer. Restriction sites needed for later cloning within the oligonucleotides are deleted. For Vkl L1 the following oligonucleotides are used:

5'PM3-VL-A-SacI

CTT GAT GAG CTC CAG ATG ACC CAG TCC CCC ARS TYC MTG TCC RCC TCC
GTG GGC GAC AGA GTG ACC (SEQ ID NO. 755)

3'PM3-VL-B

GCC GGG CTT CTG CTG AWA CCA GGC CAC GTT GGT GTC CAC GTT CTG
GGA GGC CTT GCA GGT GAY GGT CAC TCT GTC GCC (SEQ ID NO. 756)

5'PM3-VL-C

CAG CAG AAG CCC GGC MAG KCC CCT AAG KCC CTG ATC TAC TCC GCC
TCC TAC CGG TAC TCT (SEQ ID NO. 757)

3'PM3-VL-D

CAG GGT GAA GTC GGT GCC GGA CYC GGA GCC GGA GAA CCG GKM AGG
CAC GYC AGA GTA CCG GTA GGA (SEQ ID NO. 758)

5'PM3-VL-E

ACC GAC TTC ACC CTG ACC ATC TCC ARC STG CAG YCT GAG GAC YTC GCC
RMG TAC TWC TGC CAG CAG TAC GAC (SEQ ID NO. 759)

3'PM3-VL-F-BsiWI/Spel

CGA GTA ACT AGT CGT ACG CTT GAT TTC CAG CTT GGT CCC TCC GCC GAA
GGT GTA AGG GTA GGA GTC GTA CTG CTG GCA (SEQ ID NO. 760)

[0340] For Vkl A17 the oligonucleotides are as follows:

5'PM4-VL-A-SacI

CTT GAT GAG CTC GTG ATG ACC CAG TCC CCC CTG TCC CTG CCT GTG AYC
CTG GGC SAM CMG GCC TCC ATC TCC TGC CGG (SEQ ID NO. 761)

3'PM4-VL-B

AAA CCA GTG CAG GTA GGT ATT GCC GTT GGA GTG CAC CAG GGA CTG
GGA GGA CCG GCA GGA GAT GGA GGC (SEQ ID NO. 762)

5'PM4-VL-C

ACC TAC CTG CAC TGG TTT CWG CAG ARG CCT GGC CAG TCC CCT ARG
CKG CTG ATC TAC ACC GTG TCC AAC CGG (SEQ ID NO. 763)

3'PM4-VL-D

CAG GGT GAA GTC GGT GCC GGA GCC GGA GCC AGA GAA CCT GTC AGG
CAC GCC GGA GAA CCG GTT GGA CAC GGT (SEQ ID NO. 764)

5'PM4-VL-E

GGC ACC GAC TTC ACC CTG AAG ATC TCC CGG GTG GAG GCC GAA GAT
STG GGC GTG TAC TWT TGC TCC CAG TCC ACC (SEQ ID NO. 765)

3'PM4-VL-F-BsiWI/Spel

ACT CAG ACT AGT CGT ACG CTT GAT TTC CAG CTT GGT CCC TCC GCC GAA
GGT AGG CAC GTG GGT GGA CTG GGA GCA (SEQ ID NO. 766)

[0341] For Vkl A1 the following oligonucleotides are used:

5'PM8-VL-A-SacI

CTT GAT GAG CTC GTG ATG ACC CAG TCT CCA SYC TCC CTG SCT GTG ACT
CTG GGC CAG CSG GCC TCC ATC TCT TGC CGG (SEQ ID NO. 767)

3'PM8-VL-B

CCA GTG CAT GAA GGT GTT GTC GTA GGA GTC GAT GGA CTC GGA GGC
CCG GCA AGA GAT GGA GGC (SEQ ID NO. 768)

5'PM8-VL-C

ACC TTC ATG CAC TGG TWT CAG CAG ARG CCT GGC CAG YCT CCT MRC
CKG CTG ATC TWC CGG GCC TCT ATC CTG GAA (SEQ ID NO. 769)

3'PM8-VL-D

CAG GGT GAA GTC GGT GCC GGA GCC AGA GCC GGA GAA CCG GKC AGG
GAY GCC GGA TTC CAG GAT AGA GGC CCG (SEQ ID NO. 770)

5'PM8-VL-E

ACC GAC TTC ACC CTG AMA ATC TMC CST GTG GAG GCC GAS GAC GTG
GSC RYC TAC TAC TGC CAC CAG (SEQ ID NO. 771)

3'PM8-VL-F-BsiWI/SpeI

ACT CAG ACT AGT CGT ACG CTT GAT TTC CAG CTT GGT CCC TCC GCC GAA
GGT GTA AGG GTC CTC GAT GGA CTG GTG GCA GTA GTA (SEQ ID NO. 772)

[0342] Each of these primer-sets spans over the whole corresponding VL sequence.

[0343] Within each set primers are mixed in equal amounts (e.g. 1 μ l of each primer (primer stocks 20 to 100 μ M) to a 20 μ l PCR reaction) and added to a PCR mix consisting of PCR buffer, nucleotides and Taq polymerase. This mix is incubated at 94 °C for 3 minutes, 65 °C for 1 minute, 62°C for 1 minute, 59 °C for 1 minute, 56 °C for 1 minute, 52 °C for 1 minute, 50 °C for 1 minute and at 72°C for 10 minutes in a PCR cyclor. Subsequently the product is run in an agarose gel electrophoresis and the product of a size from 200 to 400 isolated from the gel according to standard methods.

[0344] Each VL PCR product is then used as a template for a standard PCR reaction using primers that incorporate N-terminal and C-terminal suitable cloning restriction sites. The DNA fragment of the correct size (for a VL approximately 330 nucleotides) is isolated by agarose gel electrophoresis according to standard methods. In this way sufficient VL DNA fragment is amplified.

[0345] The final VH3 3-11 -based VH PCR product (i.e. the repertoire of human/humanized VH) is then combined with the final Vkl L1 -based VL PCR product (i.e. the repertoire of human/humanized VL), the final VH1 1-02 -based VH PCR product (i.e. the repertoire of human/humanized VH) is combined with the final Vkl A17-based VL PCR product (i.e. the repertoire of human/humanized VL) and the final VH1 1-03 - based VH PCR product (i.e. the repertoire of human/humanized VH) is combined with the final Vkl A1-based VL PCR product (i.e. the repertoire of human/humanized VL) in the phage display vector pComb3H5Bhis, respectively. These three VH-VL combinations form three different libraries of functional scFvs from which - after display on filamentous phage - anti-PSMA binders are selected, screened, identified and confirmed as described in the following:

450 ng of the light chain fragments (Sacl-SpeI digested) are ligated with 1400 ng of the phagemid pComb3H5Bhis (Sacl-SpeI digested; large fragment). The resulting combinatorial antibody library is then transformed into 300 μ l of electro-competent Escherichia coli XL1 Blue cells by electroporation (2.5 kV, 0.2 cm gap cuvette, 25 μ FD, 200 Ohm, Biorad gene-pulser) resulting in a library size of more than 10^7 independent clones. After one hour of phenotype expression, positive transformants are selected for carbenicilline resistance encoded by the pComb3H5Bhis vector in 100 ml of liquid super broth (SB)-culture over night. Cells are then harvested by centrifugation and plasmid preparation is carried out using a commercially available plasmid preparation kit (Qiagen).

[0346] 2800 ng of this plasmid-DNA containing the VL-library (XhoI-BstEII digested; large fragment) are ligated with 900 ng of the heavy chain V-fragments (XhoI-BstEII digested) and again transformed into two 300 μ l aliquots of electro-competent E. coli XL1 Blue cells by electroporation (2.5 kV, 0.2 cm gap cuvette, 25 μ FD, 200 Ohm) resulting in a total VH-VL scFv (single chain variable fragment) library size of more than 10^7 independent clones.

[0347] After phenotype expression and slow adaptation to carbenicilline, the E. coli cells containing the antibody library are transferred into SB-carbenicilline (SB with 50 μ g/ml carbenicilline) selection medium. The E. coli cells containing the antibody library is then infected with an infectious dose of 10^{12} particles of helper phage VCSM13 resulting in the production and secretion of filamentous M13 phage, wherein phage particle contains single stranded pComb3H5Bhis-DNA encoding a scFv-fragment and displayed the corresponding scFv-protein as a translational fusion to phage coat protein III. This pool of phages displaying the antibody library is used for the selection of antigen binding entities.

[0348] For this purpose the phage library carrying the cloned scFv-repertoire is harvested from the respective culture supernatant by PEG8000/NaCl precipitation and centrifugation. Approximately 10^{11} to 10^{12} scFv phage particles are resuspended in 0.4 ml of PBS/0.1% BSA and incubated with 10^5 to 10^7 PSMA-positive human prostate cancer cell line

LNCaP (ATCC No. CRL-1740) for 1 hour on ice under slow agitation. These LNCaP cells are harvested beforehand by centrifugation, washed in PBS and resuspended in PBS/1 % FCS (containing 0.05% Na Azide). scFv phage which do not specifically bind to LNCaP cells are eliminated by up to five washing steps with PBS/1 % FCS (containing 0.05% Na Azide). After washing, binding entities are eluted from the cells by resuspending the cells in HCl-glycine pH 2.2 (10 min incubation with subsequent vortexing) and after neutralization with 2 M Tris pH 12, the eluate is used for infection of a fresh uninfected *E. coli* XL1 Blue culture (OD₆₀₀ > 0.5). The *E. coli* culture containing *E. coli* cells successfully transduced with a phagemid copy, encoding a human/humanized scFv-fragment, are again selected for carbenicilline resistance and subsequently infected with VCMS 13 helper phage to start the second round of antibody display and in vitro selection. A total of 4 to 5 rounds of selections are carried out, normally.

[0349] In order to screen for PSMA specific binders plasmid DNA corresponding to 4 and 5 rounds of panning is isolated from *E. coli* cultures after selection. For the production of soluble scFv-protein, VH-VL-DNA fragments are excised from the plasmids (XhoI-SpeI). These fragments are cloned via the same restriction sites into the plasmid pComb3H5BFlag/His differing from the original pComb3H5BHis in that the expression construct (e.g. scFv) includes a Flag-tag (DYKDDDDK) between the scFv and the His6-tag and the additional phage proteins are deleted. After ligation, each pool (different rounds of panning) of plasmid DNA is transformed into 100 µl heat shock competent *E. coli* TG1 or XLI blue and plated onto carbenicilline LB-agar. Single colonies are picked into 100 µl of LB carb (50 µg/ml carbenicilline).

[0350] *E. coli* transformed with pComb3H5BFlag/His containing a VL- and VH-segment produce soluble scFv in sufficient amounts after induction with 1 mM IPTG. Due to a suitable signal sequence, the scFv-chain is exported into the periplasma where it folds into a functional conformation.

[0351] Single *E. coli* TG1 bacterial colonies from the transformation plates are picked for periplasmic small scale preparations and grown in SB-medium (e.g. 10 ml) supplemented with 20 mM MgCl₂ and carbenicilline 50 µg/ml (and re-dissolved in PBS (e.g. 1 ml) after harvesting. By four rounds of freezing at -70°C and thawing at 37°C, the outer membrane of the bacteria is destroyed by temperature shock and the soluble periplasmic proteins including the scFvs are released into the supernatant. After elimination of intact cells and cell-debris by centrifugation, the supernatant containing the anti-PSMA scFvs is collected and used for the identification of PSMA specific binders as follows: Binding of scFvs to PSMA is tested by flow cytometry on the PSMA-positive human prostate cancer cell line LNCaP (ATCC No. CRL-1740). A periplasmic small scale preparation as described above without any grown bacteria is used as negative control.

[0352] For flow cytometry 2.5×10⁵ cells are incubated with 50 µl of scFv periplasmic preparation or with 5 µg/ml of purified scFv in 50 µl PBS with 2% FCS. The binding of scFv is detected with an anti-His antibody (Penta-His Antibody, BSA free, Qiagen GmbH, Hilden, FRG) at 2 µg/ml in 50 µl PBS with 2% FCS. As a second step reagent a R-Phycoerythrin-conjugated affinity purified F(ab')₂ fragment, goat anti-mouse IgG (Fc-gamma fragment specific), diluted 1:100 in 50 µl PBS with 2% FCS (Dianova, Hamburg, FRG) is used. The samples are measured on a FACScan (BD biosciences, Heidelberg, FRG).

[0353] Single clones are then analyzed for favourable properties and amino acid sequence. PSMA specific scFvs are converted into recombinant bispecific single chain antibodies by joining them via a Gly₄Ser₁-linker with the CD3 specific scFv I2C (SEQ ID 185) or any other CD3 specific scFv of the invention to result in constructs with the domain arrangement VH_{PSMA} - (Gly₄Ser₁)₃ - VL_{PSMA} - Gly₄Ser₁ - VH_{CD3} - (Gly₄Ser₁)₃ - VL_{CD3} or VL_{PSMA} - (Gly₄Ser₁)₃ - VH_{PSMA} - Gly₄Ser₁ - VH_{CD3} - (Gly₄Ser₁)₃ - VL_{CD3} or alternative domain arrangements. For expression in CHO cells the coding sequences of (i) an N-terminal immunoglobulin heavy chain leader comprising a start codon embedded within a Kozak consensus sequence and (ii) a C-terminal Hiss-tag followed by a stop codon are both attached in frame to the nucleotide sequence encoding the bispecific single chain antibodies prior to insertion of the resulting DNA-fragment as obtained by gene synthesis into the multiple cloning site of the expression vector pEF-DHFR (Raum et al. Cancer Immunol Immunother 50 (2001) 141-150). Transfection of the generated expression plasmids, protein expression and purification of cross-species specific bispecific antibody constructs are performed as described in chapters 24.6 and 24.7 of this example. All other state of the art procedures are carried out according to standard protocols (Sambrook, Molecular Cloning; A Laboratory Manual, 3rd edition, Cold Spring Harbour Laboratory Press, Cold Spring Harbour, New York (2001)).

[0354] Identification of functional bispecific single-chain antibody constructs is carried out by flow cytometric binding analysis of culture supernatant from transfected cells expressing the cross-species specific bispecific antibody constructs. The flowcytometric analysis is performed on the human PSMA positive prostate cancer cell line LNCaP (ATCC No. CRL-1740) as described in chapter 24.7 of this example. Only those constructs showing bispecific binding to human and macaque CD3 as well as to PSMA are selected for further use.

[0355] Cytotoxic activity of the generated cross-species specific bispecific single chain antibody constructs against PSMA positive target cells elicited by effector T cells is analyzed as described in chapter 24.8 of this example. The human PSMA positive prostate cancer cell line LNCaP (ATCC No. CRL-1740) is used as source of target cells. Only those constructs showing potent recruitment of cytotoxic activity of effector T cells against target cells positive for PSMA are selected for further use.

25. Epitope mapping of PSMA and CD3 cross-species specific bispecific single chain antibody molecules

25.1 Generation of CHO cells expressing human / rat PSMA chimeras

[0356] For mapping of the binding epitopes of PSMA cross-species specific bispecific single chain antibody molecules, chimeric PSMA proteins were generated with PSMA from two different species. This approach requires that only the PSMA protein from one species is recognized by the antibody. Here, PSMA of *rattus norvegicus*, which is not bound by the tested PSMA cross-species specific bispecific single chain antibody molecules, was used for making chimera with human PSMA. Therefore creating a chimera in the region containing the binding epitope of a PSMA cross-species specific bispecific single chain antibody leads to loss of binding of said single chain antibody to the respective PSMA construct.

[0357] The coding sequence of human PSMA as published in GenBank (Accession number NM_004476) and the coding sequence of rat PSMA (NM_057185, *Rattus norvegicus* folate hydrolase (Folh1), mRNA, National Center for Biotechnology Information, <http://www.ncbi.nlm.nih.gov/entrez>) were used for generation of the chimeric constructs.

[0358] A set of 7 chimeric cDNA constructs was designed and generated by gene synthesis according to standard protocols. In the constructs segments of the coding sequences for the amino acids 140 to 169, 191 to 258, 281 to 284, 300 to 344, 589 to 617, 683 to 690 and 716 to 750, respectively, were exchanged for the homologous sequences of rat PSMA.

[0359] Chimeric PSMA constructs were generated as described above and designated as set out in the following Table 9:

Table 9: Designation of chimeric PSMA constructs

SEQ ID (nucl/prot)	Designation
1033/1034	huPSMArat140-169
1035/1036	huPSMArat191-258
1037/1038	huPSMArat281-284
1039/1040	huPSMArat300-344
1041/1042	huPSMArat598-617
1043/1044	huPSMArat683-690
1045/1046	huPSMArat716-750

[0360] The gene synthesis fragments were designed as to contain first a Kozak site for eukaryotic expression of the construct followed by the coding sequence of the chimeric PSMA proteins, followed in frame by the coding sequence of a FLAG-tag and a stop codon. The gene synthesis fragments were also designed as to introduce restriction sites at the beginning and at the end of the fragments. The introduced restriction sites, EcoRI at the 5' end and Sall at the 3' end, were utilized in the following cloning procedures. Undesirable internal restriction sites were removed by silent mutation of the coding sequence in the gene synthesis fragments. The gene synthesis fragments were cloned via EcoRI and Sall into a plasmid designated pEF-DHFR (pEF-DHFR is described in Raum et al. Cancer Immunol Immunother 50 (2001) 141-150) following standard protocols. The aforementioned procedures were carried out according to standard protocols (Sambrook, Molecular Cloning; A Laboratory Manual, 3rd edition, Cold Spring Harbour Laboratory Press, Cold Spring Harbour, New York (2001)). A clone with sequence-verified nucleotide sequence was transfected into DHFR deficient CHO cells for eukaryotic expression of the construct. Eukaryotic protein expression in DHFR deficient CHO cells was performed as described by Kaufmann R.J. (1990) Methods Enzymol. 185, 537-566. Gene amplification of the construct was induced by increasing concentrations of methotrexate (MTX) to a final concentration of up to 20 nM MTX.

25.2 Flow cytometric binding analysis for epitope mapping of PSMA and CD3 cross-species specific bispecific single chain antibody molecules using chimeric PSMA proteins

[0361] In order to determine the binding epitope of PSMA cross-species specific bispecific single chain antibody constructs a FACS analysis was performed. For this purpose CHO cells transfected with human / rat chimeric PSMA molecules as described in Example 25.1 were used. FACS analysis with supernatant of CHO cells expressing bispecific single chain antibody constructs was performed as described herein. Detection of binding of PSMA cross-species specific bispecific single chain antibody constructs was performed using a murine Penta His antibody and as second step reagent an Fc gamma-specific antibody conjugated to phycoerythrin. Supernatant of untransfected cells was used as a negative

control.

[0362] As shown in Figure 53 all PSMA cross-species specific bispecific single chain antibody constructs tested showed binding to the chimeric constructs huPSMArat140-169, huPSMArat191-258, huPSMArat281-284, huPSMArat683-690 and huPSMArat716-750. As furthermore shown in Figure 53 there is a lack of binding for the PSMA cross-species specific bispecific single chain antibody constructs PM84-D7 \times I2C, PM29-G1 \times I2C and PM49-B9 \times I2C to the construct huPSMArat300-344, which demonstrates the presence of a major binding epitope for these constructs in the region of amino acids 300 to 344 of human PSMA. As also shown in Figure 53 there is a lack of binding for the PSMA cross-species specific bispecific single chain antibody construct PM34-C7 \times I2C to the construct huPSMArat598-617, which demonstrates the presence of a major binding epitope for this construct in the region of amino acids 598 to 617 of human PSMA.

26 Epitope mapping using a peptide scanning approach

[0363] The two PSMA BiTE antibodies PM 76-B10 \times I2C and PM 76-A9 \times I2C were cross-reactive with rat PSMA, which excluded them from mapping by using human-rat PSMA chimeras. Likewise, binding signals of PSMA BiTE antibody PM F1-A10 \times I2C on human-rat PSMA chimeras were too weak for reliable epitope mapping. These three PSMA BiTE antibodies were subjected to an alternative epitope mapping approach based on peptide scanning (Pepscan). Pepscan uses overlapping peptides of a given protein and analyses antibody binding to immobilized peptides by enzyme-linked immunosorbent assays (ELISAs). The epitope mapping experiments with PSMA BiTE antibodies were performed at the company Pepscan (Lelystad, The Netherlands). A detailed description of the method is found elsewhere (Bernard et al. 2004, J. Biol. Chem., 279: 24313 -22; Teeling et al. 2006, J Immunol., 177: 362-71). In brief, 693 different 15-mer peptides were synthesized that span the entire extracellular amino acid sequence of human PSMA and overlap with each neighbouring 15-mer peptide by 14 amino acids. These peptides were coated to ELISA wells in a 384-well plate format. For this series of experiments, anti-PSMA scFvs of the respective BiTE antibody candidates (scFv MP 9076-A9 for BiTE antibody PM 76-A9 \times I2C; scFv MP 9076-B10 for BiTE antibody PM 76-B10 \times I2C; scFv F1-A10 for BiTE antibody PM F1-A10 \times I2C) were produced in *E. coli* and used for ELISA as crude periplasmic extracts. To this end 7 ml of crude periplasmic extracts were shipped on dry ice to Pepscan (The Netherlands). Using scFv counterparts in this assay minimized the risk to pick up signals from the second non-PSMA binding specificity of the BiTE antibodies, which may lead to misinterpretation of the PSMA binding epitopes of the target binders. The scFvs were incubated with the peptides and specific binding detected using an anti-His antibody. Binding signals were measured in a 384-well ELISA reader. Results are shown in Figures 54, 55 and 56.

[0364] Of the three anti-PSMA scFv antibodies used to generate PSMA BiTE antibodies (scFv MP 9076-A9 for BiTE antibody PM 76-A9 \times I2C; scFv MP 9076-B10 for BiTE antibody PM 76-B10 \times I2C; scFv F1-A10 for BiTE antibody PM F1-A10 \times I2C) apparently two (MP 9076-A9 and MP 9076-B10) bound to a similar dominant epitope of human PSMA. This finding is supported by the close homology of the two scFv antibodies and sequence identity in their six CDRs. The peptide binding signals point to a core epitope between Thr334 to Thr339. This sequence is located in an exposed loop of the apical domain of human PSMA as is shown in Figure 57. For scFv F1-A10, a dominant epitope could be detected within the sequence LFEPPPPGYENV (amino acids 143-155 of human PSMA), which is also localized in the apical domain. The strong binding of the three antibody fragments MP 9076-A9, MP9076-B10 and F1-A10 to discrete peptides indicates recognition of a linear protein epitope rather than a carbohydrate moiety.

SEQ ID NO.	DESIGNATION	SOURCE	TYPE	SEQUENCE
1.	Human CD3ε extracellular domain	human	aa	QDGNEEMGGITQTTPYKVSISGTTVILTCTPQYPGSEILWQHNDKNI GGDEDDKNIGSDEDDHLSLKE FSELEQSGYYVVCYPRGSKPEDANFYLYLRARVCENCMEMD
2.	Human CD3ε 1-27	human	aa	QDGNEEMGGITQTTPYKVSISGTTVILT
3.	<i>Calithrix jacchus</i> CD3ε extracellular domain	<i>Calithrix jacchus</i>	aa	QDGNEEMGDTTQNPYKVSISGTTVILTCTPRYDGHGHEIKWLVNSQNKEGHEDHLLLEDFSEMEQSGY YACLSKETPAEEASHLYLYLKARVCENCVEVD
4.	<i>Calithrix jacchus</i> CD3ε 1-27	<i>Calithrix jacchus</i>	aa	QDGNEEMGDTTQNPYKVSISGTTVILT
5.	<i>Saguinus oedipus</i> CD3ε extracellular domain	<i>Saguinus oedipus</i>	aa	QDGNEEMGDTTQNPYKVSISGTTVILTCTPRYDGHGHEIKWLVNSQNKEGHEDHLLLEDFSEMEQSGY YACLSKETPAEEASHLYLYLKARVCENCVEVD
6.	<i>Saguinus oedipus</i> CD3ε 1-27	<i>Saguinus oedipus</i>	aa	QDGNEEMGDTTQNPYKVSISGTTVILT
7.	<i>Saimiri sciureus</i> CD3ε extracellular domain	<i>Saimiri sciureus</i>	aa	QDGNEEIGDTTQNPYKVSISGTTVILTCTPRYDGHGHEIKWLVDNQKEGHEDHLLLEDFSEMEQSGY YACLSKETPTEEASHLYLYLKARVCENCVEVD
8.	<i>Saimiri sciureus</i> CD3ε 1-27	<i>Saimiri sciureus</i>	aa	QDGNEEIGDTTQNPYKVSISGTTVILT
9.	CDR-L1 of F6A	artificial	aa	GSSTGAVTSGYYPN
10.	CDR-L2 of F6A	artificial	aa	GTKFLAP
11.	CDR-L3 of F6A	artificial	aa	ALWYSNRWV
12.	CDR-H1 of F6A	artificial	aa	IYAMN
13.	CDR-H2 of F6A	artificial	aa	RIRSKYNNYATYYADSVKS
14.	CDR-H3 of F6A	artificial	aa	HGNFGNSYVSEFFAY
15.	VH of F6A	artificial	aa	EVQLVESGGGLVQPGGSLKLSAASGFTFNLYAMNWRQAPGKGLEWVARIRSKYNNYATYYADS VKSRFTISRDDSKNTAYLQMNNLKTEDTAVYICVRHGNFGNSYVSEFFAYWGQGITLVSS
16.	VH of F6A	artificial	nt	CAGCTCAGCTGCTCCAGCTCTCGACGACGATTGCTCCACCTCGACCGTCACTTGAACCTCTCATG TGACGCTCTGGATTCACTTCAATATCTACGCCATGAACCTGGTCCGCGGCTCCAGGAAAGG GTTTGAATGGTTGCTCGCATAGAAGTAAATAATAATATGCAACATATTATGCCGATTCA GTGAAAAGCAGGTTACCATCTCCAGAGATGATCAAAAAACACTGCCTATCTACAAATGAACAA CTTGAAAACACTGAGGACACTGCCGTGTACTGTGTGAGACATGGGAACCTTCGGTAAAGCTACG TATCCTTCTTCGCTTACTGGGGCCAGGACTCTGCTACCGTCTCCTCA
17.	VL of F6A	artificial	aa	QTVVTEPSLTVSPGGTTLTCGSSTGAVTSGYYPNWWQKPGQAPRGLIGGKFLAPGTPAPFS

18.	VL of F6A	artificial	nt	<p>GSLGGKAAALTLSGVQPEDEAEYYCALWYSNRWVFGGKLTIVL</p> <p>CAGACTGTTGTGACTCAGGAACCTTCACTACCGTATACCTGGTGAACAGTCACACTCATTG TGGTCCTCGACTGGGCTGTTACATCTGGCTACTACCAAACTGGTCCAAACAAACAGGTC AGCAACCCGCTGGTCTAATAGGTGGACTAACTTCTCGCCCGGTACTCTCCAGATTCTCA GGTCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATCAGGCAGA ATATTACTGTGCTCTATGGTACAGCAACCGCTGGGTGTTCCGTGGAGGAACCAAACTCACTGCTCC TA</p>
19.	VH-P of F6A	artificial	aa	<p>EVQLVESGGGLVQPGGSLKLSCAASGFTFNIIYAMNWRQAPGKLEWVARIRSKYNNYATYYADS VKSRFTISRDTSKNTAYLQMNNLKTEDTAVYCVRHGNGFSYVSFFAYWGQGTLVTVSS</p>
20.	VH-P of F6A	artificial	nt	<p>GAGGTGCAGCTGCTCGAGTCTGGAGGAGGATTGGTGCAGCCTGGAGGTCACTTGAACCTCTCATG TGCAGCCTCTGGATTCACTTCAATATCTACGCCATGAACCTGGTCCGCCAGGCTCCAGCAAGG GTTTGAATAGGTGCTCGCATAGAAGTAAATATAATAATATATGCAACATATTATGCCGATTCA GTGAAAAGCAGGTTCACTCTCCAGAGATGATTCAAAAAACAATGCTCTACAAATGAACAA CTTGAAAACCTGAGGACACTGCCGTGTACTGTGTGAGACATGGGAACCTCGGTAAATAGCTACG TATCCTTCTTCGCTTACTGGGGCCAGGGACTCTGGTCACCGTCTCCTCA</p>
21.	VL-P of F6A	artificial	aa	<p>ELVVTQEPSLITVSPGGTVTLTCGSSTGAVTSYYPNWWQKPGQAPRGLIGGTKFLAPGTPARFS GSLGGKAAALTLSGVQPEDEAEYYCALWYSNRWVFGGKLTIVL</p>
22.	VL-P of F6A	artificial	nt	<p>GAGTCGTTGTGACTCAGGAACCTTCACTACCGTATACCTGGTGGAAACAGTCACACTCATTG TGGTCCTCGACTGGGCTGTTACATCTGGCTACTACCAAACTGGTCCAAACAAACAGGTC AGCAACCCGCTGGTCTAATAGGTGGACTAACTTCTCGCCCGGTACTCTCCAGATTCTCA GGTCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGA ATATTACTGTGCTCTATGGTACAGCAACCGCTGGGTGTTCCGTGGAGGAACCAAACTCACTGCTCC TA</p>
23.	VH-VL of F6A	artificial	aa	<p>EVQLVESGGGLVQPGGSLKLSCAASGFTFNIIYAMNWRQAPGKLEWVARIRSKYNNYATYYADS VKSRFTISRDTSKNTAYLQMNNLKTEDTAVYCVRHGNGFSYVSFFAYWGQGTLVTVSSGGGGS GGSGGGGGSQTVVTOEPSLITVSPGGTVTLTCGSSTGAVTSYYPNWWQKPGQAPRGLIGGTKF LAPGTPARFSGSLLGKAAALTLSGVQPEDEAEYYCALWYSNRWVFGGKLTIVL</p>
24.	VH-VL of F6A	artificial	nt	<p>GAGTGCAGCTGCTCGAGTCTGGAGGAGGATTGGTGCAGCCTGGAGGTCACTTGAACCTCTCATG TGCAGCCTCTGGATTCACTTCAATATCTACGCCATGAACCTGGTCCGCCAGGCTCCAGCAAGG GTTTGAATAGGTGCTCGCATAGAAGTAAATATAATAATATGCAACATATTATGCCGATTCA GTGAAAAGCAGGTTCACTCTCCAGAGATGATTCAAAAAACAATGCTCTACAAATGAACAA CTTGAAAACCTGAGGACACTGCCGTGTACTGTGTGAGACATGGGAACCTCGGTAAATAGCTACG TATCCTTCTTCGCTTACTGGGGCCAGGGACTCTGGTCACTCTCCTCAGGTGGTGGTGGTCTCT GGCGGGGGGCTCCGGTGGTGGTGGTCTCAGACTGTGTGACTCAGGAACCTTCACTCACCGT ATCACTGGTGAACAGTCACACTCTGTGGTCTCGACTGGGCTGTACATCTGGGTACT ACCCAAACTGGTCCAAACAAACAGGTCAGGCACCCCGTGGTCTAATAGGTGGGACTAAGTTC CTCGCCCCGGTACTCTCTGCCAGATTCTCAGGCTCCCTGCTTGAGGCAAGGCTGCCCTCACCT</p>

				CTCAGGGGTACAGCCAGAGGATGAGGCAGAATATTACTGTGCTCTATGGTACAGCAACCGCTGGG TGTTCCGTGGAGGAACCAACTGACTGTCTTA
25.	VH-VL-P of F6A	artificial	aa	EVQLLESGGGLVQPFGSLKLSCAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYYADS VKSRFTISRDDSKNTAYLQMNLLKTEDTAVYCVRHGNFGNSYVFFAYWGQGLVTVSSGGGGS GGGGGGGGSEIVVTEPSLTVSPGGTVTLTCCSSTGAVTSGYYPNWWQKPGQAPRGLIGGTFK LAPGTPAFPSGLLGGKAALTLSGVQPEDEAEYVYCALWYSNRWVFGGKLTVL
26.	VH-VL-P of F6A	artificial	nt	GAGGTGAGCTGCTCGAGTCTGGAGGAGGATTGGTGCAGCCTGGAGGGTCATTGAAACTCTCATG TGCAGCCTCTGGATTACCTTCAATATCTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGGAATGGGTGCTCGCATAGAAGTAATAATAATAATAATATGCAACATATTATGCCGATTCA GTGAAAAGCAGGTTACCATCTCCAGAGATGATCAAAAACACTGCCTATCTACAAATGAACAA CTTGAAAACCTGAGGACACTGCCGTGTAATACTGTGTGAGACATGGGAACCTCGGTAAATAGCTACG TATCCTTCTTCGCTTACTGGGGCCAAAGGACTCTGGTCAACCGTCTCCTCAGGTGGTGGTCTCT GGCGGGCGGCTCCGGTGGTGGTCTGAGTCTGTGACTCAGGAACCTTCACTCACCCT ATCACCCTGGTGGAAACAGTCACACTCACTTGTGGTCTCGACTGGGCTGTACACTGGCTACT ACCCAAACTGGGTCCAAACAAACAGGTACGACGCCCTGGTCTTAATAGGTGGACTAAGTTC CTCGCCCCGGTACTCTCGCCAGATTCTCAGGCTCCCTGCTGGAGGCAAGGCTGCCCTCACCT CTCAGGGGTACAGCCAGAGGATGAGGCAGAATATTACTGTGCTCTATGGTACAGCAACCGCTGGG TGTTCCGTGGAGGAACCAACTGACTGTCTTA
27.	CDR-L1 of H2C	artificial	aa	GSSTGAVTSGYYPN
28.	CDR-L2 of H2C	artificial	aa	GTKFLAP
29.	CDR-L3 of H2C	artificial	aa	ALWYSNRWV
30.	CDR-H1 of H2C	artificial	aa	KYAMN
31.	CDR-H2 of H2C	artificial	aa	RIRSKYNNYATYYADSVKD
32.	CDR-H3 of H2C	artificial	aa	HGNFGNSYISYWAY
33.	VH of H2C	artificial	aa	EVQLVESGGGLVQPFGSLKLSCAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYYADS VKDRFTISRDDSKNTAYLQMNLLKTEDTAVYCVRHGNFGNSYISYWAYWGQGLVTVSS
34.	VH of H2C	artificial	nt	GAGTGCAGCTGGTCTGAGTCTGGAGGAGGATTGGTGCAGCCTGGAGGGTCATTGAAACTCTCATG TGCAGCCTCTGGATTACCTTCAATAAGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGGAATGGGTGCTCGCATAGAAGTAATAATAATAATAATATGCAACATATTATGCCGATTCA GTGAAAAGCAGGTTACCATCTCCAGAGATGATCAAAAACACTGCCTATCTACAAATGAACAA CTTGAAAACCTGAGGACACTGCCGTGTAATACTGTGTGAGACATGGGAACCTCGGTAAATAGTACA TATCCTACTGGGCTTACTGGGGCCAAAGGACACTCTGCTCACCCTCTCCTCA

35.	VL of H2C	artificial	aa	QTVVTQEPSTLTVSPGGTVTLTCGSSTGAVTSGYYPNWVQKPGQAPRGLIGGTKFLAPGFARFS GSLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGTKLTVL
36.	VL of H2C	artificial	nt	CAGACTGTTGTGACTCAGGAACCTTCACTCACCGTATCACTGGTGAACAGTCACACTCACTTG TGGCTCCTCGACTGGGCTGTATACATCTGGTACTACCCAACTGGTCCAAACAAACAGGTC AGGCACCCCGTGGTCTAATAGTGGGACTAAGTCTCCTCCCGGCTACTCCTGCCAGATTCTCA GGCTCCCTGCTTGGAGGCAAGGCTGCCCTCCTCAGGGGTACAGCCAGGATGAGGCAGA ATATTACTGTGCTCTATGGTACAGCAACCGCTGGGTGTTCCGGTGGAGGAACCAAACTGACTGTCC TA
37.	VH-P of H2C	artificial	aa	EVQLLESGLVQPGGSLKLSCAASGFTFNKYAMNWNVRQAPGKLEWVARIRSKYNNYATYYADS VKDRFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFGNSYISYWAYWGQGLTVYSS
38.	VH-P of H2C	artificial	nt	GAGTGCAGCTGCTCGAGTCTGGAGGAGGATGGTGCAGCCTGGAGGGTCATTGAAACTCTCATG TGCAGCCTCTGGATTCACTTCAATAAGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAATATAATATATGCAACATATTATGCCGATTCA GTGAAAGACAGGTTCAACATCTCCAGAGATGATCAAAAACACTGCCATCTACAAATGAACAA CTTGAAAACCTGAGGACACTGCCGTGTACTGTGTGAGACATGGCACTTCGGTAACTAGCTACA TATCCTACTGGGCTTACTGGGGCCAGGGACTGCTGGTCACTCTCCTCA
39.	VL-P of H2C	artificial	aa	ELVVTQEPSTLTVSPGGTVTLTCGSSTGAVTSGYYPNWVQKPGQAPRGLIGGTKFLAPGTPARFS GSLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGTKLTVL
40.	VL-P of H2C	artificial	nt	GAGTCGTTGTGACTCAGGAACCTTCACTCACCGTATCACTGGTGAACAGTCACACTCACTTG TGGCTCCTCGACTGGGCTGTATACATCTGGCTACTACCCAACTGGTCCAAACAAACAGGTC AGGCACCCCGTGGTCTAATAGTGGGACTAAGTCTCCTCCCGGCTACTCCTGCCAGATTCTCA GGCTCCCTGCTTGGAGGCAAGGCTGCCCTCACTCCTCAGGGGTACAGCCAGGATGAGGCAGA ATATTACTGTGCTCTATGGTACAGCAACCGCTGGGTGTTCCGGTGGAGGAACCAAACTGACTGTCC TA
41.	VH-VL of H2C	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWNVRQAPGKLEWVARIRSKYNNYATYYADS VKDRFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFGNSYISYWAYWGQGLTVYSSGGGGS GGGSGGGGSQTVVTQEPSTLTVSPGGTVTLTCGSSTGAVTSGYYPNWVQKPGQAPRGLIGGTKF LAPGTPARFSCSLLCCKAALTLGVQPEDEAEYYCALWYSNRWVFGGTKLTVL
42.	VH-VL of H2C	artificial	nt	GAGTCCAGCTGGTCGAGTCTGGAGGAGGATGGTGCAGCCTGGAGGGTCATTGAACCTCTCATG TGACGCTCTGGATTCACTTCAATAAGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAATATAATATATGCAACATATTATGCCGATTCA GTGAAAGACAGGTTCAACATCTCCAGAGATGATCAAAAACACTGCCATCTACAAATGAACAA CTTGAAAACCTGAGGACACTGCCGTGTACTGTGTGAGACATGGGAACCTTCGGTAACTAGCTACA TATCCTACTGGGCTTACTGGGGCCAGGACTGCTGGTCACTCCTCCTCAGGTGGTGGTGTCT GGGGGGGGGCTCCGGTGGTGGTGTCTCAGACTGTGTGACTCAGGAACCTTCACTCACCGT ATCACCTGGTGAACAGTCACACTCACTTGTGGCTCCTCGACTGGGCTGTACATCTGGCTACT ACCCAAACTGGGTCCACAAACACAGGTCAGGCACCCCGTGGTCTAATAGGTGGGACTAAGTTC

				CTGCCCCCGGTACTCTCGCAGATTCTCAGGCTCCCTGCTGGAGGCAAGGCTGCCCTCACCCCT CTCAGGGGTACAGCCAGAGGATGAGGCAGATAATCTGTGCTCTATGGTACAGCAACCGCTGGG TGTTCCGTGGAGAACCAACTGACTGTCCTA
43.	VH-VL-P of H2C	artificial	aa	EVQLLESGGGLVQPFGSLKLSCAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADS VKDRFTISRDDSKNTAYLOMNNLKTEDTAVYICVRHGNFGNSYISYWAYWGQGLTVTVSSGGGS GGGSGGSGSELVVTQEPSTLVSPFGTVTLTSGSTGAVTSYYPNWWQKPGQAPRGLIGGTFK LAPGTPARFSGSLGGKAALTLSGVQPEDEAEYICALWYSNRWVEGGTKLTVL
44.	VH-VL-P of H2C	artificial	nt	GAGTGCAGCTGCTCGAGTCTGGAGGAGGATGGTGCAGCCTGGAGGTCATTGAAACTCTCATG TGCAGCCTCTGGATTCACTTCAATAAGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAATAATAATATGCAACATATTATGCCGATTCA GTGAAAGACAGGTTACCATCTCCAGAGATGATCAAAAAACACTGCCCTATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTCTGTGAGACATGGGAACCTTCGGTAATAGCTACA TATCCTACTGGGCTTACTGGGGCCAGGACTCTGGTCACTCCCTCAGTGGTGGTCTCT GGCGGCGGCTCCGGTGGTGGTCTGAGCTGCTGAGTCAAGAACCTTCACTCACCGT ATCAGCTGGTGAACAGTCACTCACTTCTGGCTCCTCGACTGGGCTGTTACATCTGGCTACT ACCCAACTGGGTCCAAACAAACAGGTCAGGCACCCCGTGGTCTAATAGGTGGGACTAAGTTC CTGCCCCCGGTACTCTGCCAGATTCTCAGGCTCCCTGCTGGAGGCAAGGCTGCCCTCACCCCT CTCAGGGGTACAGCCAGAGGATGAGGCAGATAATCTGTGCTCTATGGTACAGCAACCGCTGGG TGTTCCGTGGAGGAACCAACTGACTGTCTCTA
45.	CDR-L1 of H1E	artificial	aa	GSSTGAVTSGYYPN
46.	CDR-L2 of H1E	artificial	aa	GTKFLAP
47.	CDR-L3 of H1E	artificial	aa	ALWYSNRWV
48.	CDR-H1 of H1E	artificial	aa	SYAMN
49.	CDR-H2 of H1E	artificial	aa	RIRSKYNNYATYYADSVKG
50.	CDR-H3 of H1E	artificial	aa	HGNFGNSYLSFWAY
51.	VH of H1E	artificial	aa	EVQLVLESGGGLVQPFGSLKLSCAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADS VKGRFTISRDDSKNTAYLOMNNLKTEDTAVYICVRHGNFGNSYLSFWAYWGQGLTVTVSS
52.	VH of H1E	artificial	nt	GAGTGCAGCTGGTTCAGTCTGGAGGAGGATGGAGCAGCCTGGAGGTCATTGAAACTCTCATG TGCAGCCTCTGGATTCACTTCAATTCGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAATAATAATATGCAACATATTATGCCGATTCA GTGAAAGGAGGTTACCATCTCCAGAGATGATCAAAAAACACTGCCCTATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTCTGTGAGACATGGGAACCTTCGGTAATAGCTACC TATCCTCTGGGCTTACTGGGGCCAGGACTCTGGTCACTCCCTCTCCTC
53.	VL of H1E	artificial	aa	QTVVTQEPSTLVSPFGTVTLTSGSTGAVTSYYPNWWQKPGQAPRGLIGGTFKFLAPGTFAPFS GSLGKGKAALTLSGVQPEDEAEYICALWYSNRWVEGGTKLTVL
54.	VL of H1E	artificial	nt	CAGACTGTTGTGACTCAGGAACCTTCACCTACCCGATACCTGGTGGAAACAGTCACACTCACTTG

					<p>TGGTCTCTGACTGGGCTGTTACATCTGGCTACTACCCAAACTGGGTCCAACAAAACACGATC AGGCACCCCGTGGTCTAATAGGTGGACTAAGTTCCTCGCCCGGCTACTCCTCCAGATTCTCA GGCTCCCTGCTTGGAGGCAAGGCTGCCCTACCTCTCAGGGGTACAGCCAGAGGATGAGGAGA ATATTACTGTGCTCTATGGTACAGCAACCGCTGGGTGTTCCGTGGAGGAACCAAACTGACTGCC TA</p>
55.	VH-P of H1E	artificial	aa		<p>EVQLVESGGGLEQPGGSLKLSCAASGFTTNSYAMNWVRQAPKGLEWVARIRSKYNNYATYYADS VKGRFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNGFNSYLSFWAYWGQGLTVVSS</p>
56.	VH-P of H1E	artificial	nt		<p>GAGGTGAGCTGCTCGAGTCTGGAGGAGGATTGGAGCAGCCTGGAGGGTCATTGAAACTCTCATG TGCAGCCTCTGGATTACCTTCAATTCGTACGCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAAATATAATAATATATGCAACATATTATGCCGATTCA GTGAAAGGAGGTTTACCATCTCCAGAGATGATCAAAAACAACCTGCCTATCTACAAATGAACAA CTTGAAAACGTAGGACACTGCCGTGACTGTTGTGAGACATGGAACTTCGGTAATAGCTACC TATCCTTCTGGCTTACTGGGGCCAGGGACTCTGGTCAACCTCTCCTCA</p>
57.	VL-P of H1E	artificial	aa		<p>ELVVTQEPSLTVSPGGTVTLTCGSTGAVTSGYYPNWVQKPGQAPRGLIGGTKFLAPTPARFS GSLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGTKLTVL</p>
58.	VL-P of H1E	artificial	nt		<p>GAGCTCGTTGTGACTCAGGAACCTTCACTACCCGTATCACCTGGTGGAAACAGTCACACTCATTTG TGGTCTCTGACTGGGCTGTTACATCTGGCTACTACCCAAACTGGGTCCAACAAAACACGATC AGCACCCCGTGGTCTAATAGGTGGACTAACTTCTCGCCCGGCTACTCCTGCCAGATTCTCA GGTCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGA ATATTACTGTGCTCTATGGTACAGCAACCCGTGGGTGTTCCGTGGAGGAACCAAACTGACTGCC TA</p>
59.	VH-VL of H1E	artificial	aa		<p>EVQLVESGGGLEQPGGSLKLSCAASGFTTNSYAMNWVRQAPKGLEWVARIRSKYNNYATYYADS VKGRFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNGFNSYLSFWAYWGQGLTVVSSGGGGS GGGSGGGGSGTVVTVQEPSLTVSPGGTVTLTCGSSTGAVTSGYYPNWVQKPGQAPRGLIGTKF LAPGTPARFSGSLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGTKLTVL</p>
60.	VH-VL of H1E	artificial	nt		<p>GAGGTGAGCTGCTCGAGTCTGGAGGAGGATTGGAGCAGCCTGGAGGGTCATTGAAACTCTCATG TGCAGCCTCTGGATTACCTTCAATTCGTACGCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAAATATAATAATATATGCAACATATTATGCCGATTCA GTGAAAGGAGGTTTACCATCTCCAGAGATGATCAAAAACAACCTGCCTATCTACAAATGAACAA CTTGAAAACGTAGGACACTGCCGTGACTGTTGTGAGACATGGAACTTCGGTAATAGCTACC TATCCTTCTGGCTTACTGGGGCCAGGGACTCTGGTCAACCTCTCCTCAGGTGGTGGTGTCT GGCGGGGGGCTCCGGTGGTGGTCTCAGACTGTTGTGACTCAGGAACCTTCACTCACCGT ATCACCTGGTGCACACAGTCACACTCTCGCTCCTCCACTGGGCTGTTACATCTCGCTACT ACCCAAACTGGGTCCAACAAAACAGGTACGACCCCGTGGTCTAATAGGTGGGACTAAGTTC CTGCCCCCGGTACTCCTGCCAGATTCTCAGCTCCCTGCTGGAGGCAAGGCTGCCCTCACCT CTCAGGGGTACAGCCAGAGGATGAGGCAGAAATATTACTGTGCTCTATGGTACAGCAACCCGTGGG TGTTCCGTGGAGGAACCAAACTGACTGTCTTA</p>

61.	VH-VL-P of H1E	artificial	aa	EVQLVESGGGLVQPGGSLKLSKAASGFTFENRYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADS VKGRFTISRDDSKNTAYLQMNLLKTEDTAVYCVRHGTFNYSLSFWYWGQGLTVTVSSGGGGS GGGSGGGSELVVTQEPSTLTVSPGGTVTLTCSSTGAVTSYYPNWVQKPGQAPRGLIGTKF LAPTPARFSGSLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGLTLTVL
62.	VH-VL-P of H1E	artificial	nt	GAGTGCAGCTGCTCGAGTCTGGAGGAGGATTGGACGAGCTTGAGGGTCATTGAAACTCTCATG TGAGCCTCTGGATTACCTTCAATTCGTACGCGCATGAATGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTTCGTCCGATAAGAAGTAATAATAATATATGCAACATATTATGCCGATTCA GTGAAAGGAGGTTACCATCTCCAGAGATGATCAAAAAACACTGCCTATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTACTGTGTGAGACATGGAACTTCGGTAAATAGCTACC TATCCTTCTGGCTTACTGGGGCCAAAGGACTCTGGTCACCGTCTCCTCAGGTGGTGGTCTT GGGGCGGGCTCCGGTGGTGGTCTGAGCTCGTGTGACTCAGGAACCTTCACTCACCGT ATCACCTGGTGAACAGTCACACTCACTTGTGCTCCTCGACTGGGCTGTACATCTGGCTACT ACCCAAACTGGGTCCCAACAAACAGGTCAGGTCAGGCAACCCCTGCTTGTAGGTGGGACTAAGTTC CTCGCCCTCCGCTACTCTGCCAGATTCTCAGGCTCCTGCTTGGAGGCAAGGCTGCCCTCACCT CTCAGGGGTACAGCCAGAGGATGAGGCAGATAATACTGTCTATGTGTACAGCAACCGTGGG TGTTCGGTGGAGGAAACCAACTGACTGTCTCTA
63.	CDR-L1 of G4H	artificial	aa	GSSTGAVTSYYPN
64.	CDR-L2 of G4H	artificial	aa	GTKFLAP
65.	CDR-L3 of G4H	artificial	aa	ALWYSNRWV
66.	CDR-H1 of G4H	artificial	aa	RYAMN
67.	CDR-H2 of G4H	artificial	aa	RIRSKYNNYATYYADSVKG
68.	CDR-H3 of G4H	artificial	aa	HGNFGNSYLSYFAY
69.	VH of G4H	artificial	aa	EVQLVESGGGLVQPGGSLKLSKAASGFTFENRYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADS VKGRFTISRDDSKNTAYLQMNLLKTEDTAVYCVRHGTFNYSLSFWYWGQGLTVTVSS
70.	VH of G4H	artificial	nt	GAGTGCAGCTGGTCTGAGTCTGGAGGAGGATTGGTGCAGCTTGAGGGTCATTGAAACTCTCATG TGAGCCTCTGGATTACCTTCAATCGTACGCGCATGAATGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTTCGTCCGATAAGAAGTAATAATAATAATATGCAACATATTATGCCGATTCA GTGAAAGGAGGTTACCATCTCCAGAGATGATCAAAAAACACTGCCTATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTACTGTGTGAGACATGGAACTTCGGTAAATAGCTACT TATCCTACTTCGCTTACTGGGGCCAAAGGACTCTGGTCACCGTCTCCTCA
71.	VL of G4H	artificial	aa	QTVVTQEPSTLTVSPGGTVTLTCSSTGAVTSYYPNWVQKPGQAPRGLIGTKFLAPGTPARFS GSLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGGLTLTVL
72.	VL of G4H	artificial	nt	CAGACTGTTGTGACTCAGGAACCTTCACTACCGTATCACTGGTGGAAACAGTCACACTCACTTG TGGCTCCTCGACTGGGCTGTGTACATCTGGCTACTACCCAAACTGGTCCAAACAAACAGGTC AGGCACCCCGTGGTCTAATAGGTGGGACTAAGTTCCTCGCCCGGCTACTCTGCGAGATTCTCA GGCTCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGA

					ATATTACTGTGCTCTATGGTACAGCAACCGCTGGGTGTTTCGGTGGAGGAACCAAACTGACTGTCC TA
73.	VH-P of G4H	artificial	aa		EVQLLESGGGLVQPGGSLKLSKAASGFTFNRYAMNVRQAPGKGLEWVARIRSKYNNYATYYADS VKGRFTISRDDSKNTAYLQMNILKTEDTAVYCVRHGNFGNSYLSYFAYWGQGLVTVSS
74.	VH-P of G4H	artificial	nt		GAGGTGCAGCTGCTCGAGTCTGGAGGAGGATTGGTGCAGCCTGGAGGGTCATTGAAACTCTCATG TGCAGCCTCTGGATTACCTTCAATCGCTACGCCATGAAGTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAATAATAATATATGCAACATATATATGCCGATTCA GTGAAAGGGAGGTTACCATCTCCAGAGATGATTCAAAAACACTGCCATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTAATCTGTGTGAGACATGGAACTTCGGTAAATAGCTACT TATCCTACTTCTGCTTACTGGGGCCAGGACTCTGGTCACCGTCTCCTCA
75.	VL-P of G4H	artificial	aa		ELVVTQEPSTLTVSPGGTVTLTCSSTGAVTSGYYPNWWQKPGQAPRGLIGGKFLAPGTPARFS GSLGGKAAITLSGVQPEDEAEYYCALWYSNRWVFGGKLTIVL
76.	VL-P of G4H	artificial	nt		GAGTCTGTTGTACTCAGGAACCTTCACTACCGTATACCTGGTGAACAGTCACTCACTTGTG TGGTCTCTGACTGGGCTGTACATCTGCTACTACCCAACTGGTCCAAACAAACACAGGTC AGCACCCCGTGGTCTAATAGGTGGGACTAAGTCTCTGCCCCGGTACTCTCCGACGATTCTCA GGTCCCTGCTTGGAGGCAAGGCTGCCCTCACCCTCTCAGGGGTACAGCCAGAGGATGAGGCAGA ATATTACTGTGCTCTATGGTACAGCAACCGCTGGGTGTTTCGGTGGAGGAACCAAACTGACTGTCC TA
77.	VH-VL of G4H	artificial	aa		EVQLLESGGGLVQPGGSLKLSKAASGFTFNRYAMNVRQAPGKGLEWVARIRSKYNNYATYYADS VKGRFTISRDDSKNTAYLQMNILKTEDTAVYCVRHGNFGNSYLSYFAYWGQGLVTVSSGGGGS GGGSGGGGSQTVVTQEPSTLTVSPGGTVTLTCSSTGAVTSGYYPNWWQKPGQAPRGLIGGKTF LAPGTPARFSGLLGGKAAITLSGVQPEDEAEYYCALWYSNRWVFGGKLTIVL
78.	VH-VL of G4H	artificial	nt		GAGGTGCAGCTGGTCTGAGTCTGGAGGAGGATTGGTGCAGCCTGGAGGGTCATTGAACTCTCATG TGCAGCCTCTGGATTACCTTCAATCGCTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAATAATAATAATATGCAACATATATGCGGATTCA GTGAAAGGAGGTTACCATCTCCAGAGATGATTCAAAAACACTGCCATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTAATCTGTGTGAGACATGGAACTTCGGTAAATAGCTACT TATCCTACTTCGCTTACTGGGGCCAGGACTCTGTCACCGTCTCCTCAGCTGGTGGTGGTCTT GGCGGGGGGCTCCGGTGGTGGTCTCAGACTGTTGTGACTCAGGAACCTTCACTACCCGT ATCACCTGGTGAACAGTCACACTCACTTGTGGTCTCTGACTGGGCTGTACACTCTGGCTACT ACCCAAACTGGTCCAAACAAACAGGTCAGGCAACCCGCTGGTCTAATAGTGGGACTAAGTTC CTCGCCCCGGTACTCTCTGCCAGATTCTCAGGCTCCCTGCTGGAGGCAAGGCTGCCCTCACCCCT CTCAGGGGTACACCCACACCATGAGGCCAATAATAATACTCTCTATGTTACACCAACCCGCTGGG TGTTGGGTGAGGAACCAAACTGACTGTCTA
79.	VH-VL-P of G4H	artificial	aa		EVQLLESGGGLVQPGGSLKLSKAASGFTFNRYAMNVRQAPGKGLEWVARIRSKYNNYATYYADS VKGRFTISRDDSKNTAYLQMNILKTEDTAVYCVRHGNFGNSYLSYFAYWGQGLVTVSSGGGGS GGGSGGGGSELVVTQEPSTLTVSPGGTVTLTCSSTGAVTSGYYPNWWQKPGQAPRGLIGGKTF

80.	VH-VL-P of G4H	artificial	nt	LAPGTPARFSGSLGKAAALTLGSGVQPEDEAEYYCALWYSNRWVFGGKLTVL GAGGTGAGCTGCTCAGTCTGGAGGAGGATTGGTGAGCTGGAGGGTCATTGAAACTCTCATG TGCAGCCTCTGGATTCACTTCAATCGCTACGCTAGCTGAGCTGGTCCGCCAGGTCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAATATATAATATATGCAACATATTATGCCGATTCA GTGAAAGGGAGGTTCAACATCTCCAGAGATGATTCAAAAACACTGCCCTATCTACAATGAACAA CTTGAAAACGTAGGACACTGCCGTGTAAGTCTGTGTGAGACATGGAACTTCGGTAATAGCTACT TATCCTACTTCGCTTACTGGGGCAAGGACTCTGTGACCGCTCTCTCAGGTGGTGGTGTCT GGGGCGGGCTCCGGTGGTGGTCTGAGCTCGTGTGACTCAGGAACCTTCACTCACCCT ATCACCTGGTGAACAGTCACTCACTTGTGGCTCTCGACTGGGCTGTACATGTGGCTACT ACCCAACTGGTCCAAACAAACAGGTCAAGGACCCCGTGTCTAATAGGTGGACTAAGTTC CTGCCCCCGGTACTCTCGCAGATTCTCAGGCTCCCTGCTTGGAGGCAAGGCTGCCCTCACCT CTCAGGGGTACAGCAGAGGATGAGGAGAATATTACTGTCTCTATGTGTCTATGGTACAGCAACCGCTGGG TGTCGGTGGAGGACAAACTGACTGTCTTA
81.	CDR-L1 of A2J	artificial	aa	RSSTGAVTSGYYPN
82.	CDR-L2 of A2J	artificial	aa	ATDMRPS
83.	CDR-L3 of A2J	artificial	aa	ALWYSNRWV
84.	CDR-H1 of A2J	artificial	aa	VYAMN
85.	CDR-H2 of A2J	artificial	aa	RIRSKYNNYATYYADSVKK
86.	CDR-H3 of A2J	artificial	aa	HCNFCNSYLSWWAY
87.	VH of A2J	artificial	aa	EVQLVESGGGLVQPGGSLKLSKAASGFTFNVYAMNWVQAPGKGLEWVARIRSKYNNYATYYADS VKRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGFGNSYLSWWAYWGQGLTVSS
88.	VH of A2J	artificial	nt	GAGGTGACGCTGGTCCAGTCTGAGGAGGATTGGTGACGCTGGGTCGAGGCTCATTTGAAACTCTCATG TGCAGCCTCTGGATTCACTTCAATGTCTACGCCATGAATGAGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAATATAATAATATGCAACATATTATGCGATTCA GTGAAAAGAGGTTCAACATCTCCAGAGATGATTCAAAAACACTGCCCTATCTACAATGAACAA CTTGAAAACGTAGGACACTGCCGTGTAAGTCTGTGTGAGACATGGAACTTCGGTAATAGCTACT TATCCTGGTGGGCTTACTGGGGCAAGGACTCTGGTCACTCTCTCTCA
89.	VL of A2J	artificial	aa	QTVVTQEPSTVSPGGTVTLTCRSSTGAVTSGYYPNWVQKPGQAPRGLIGATDMRPSGTPARFS GSLGKAAALTLGSGVQPEDEAEYYCALWYSNRWVFGGKLTVL
90.	VL of A2J	artificial	nt	CAGACTGTTGTGACTCAGCAACCTTCACTCACCTACCTGGTGAACAGTCACACTCACTTG TCGCTCTCGACTGGGCTGTACATCTGGCTACTACCAAACTGGGTCCACAAAACCCAGGTC AGCACCCCGTGGTCTAATAGTGCCACTGACATGAGGCCCTCTGGTCTCTGCGAGATTCTCA GGCTCCCTGCTTGGAGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGA ATATTACTGTGCTCTATGTTACAGCAACCGCTGGGTGTCTGGTGGAGAACCAACTGACTGTCC TA
91.	VH-P of A2J	artificial	aa	EVQLVESGGGLVQPGGSLKLSKAASGFTFNVYAMNWVQAPGKGLEWVARIRSKYNNYATYYADS

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5	55					<p>GTTTGAATGGGTGCTGCATAAGAAGTAATAATAATATGCAACATATTATGCCGATTCA GTGAAAAGAGTTCAACATCTCCAGAGATGATTCAAAAAACAACCTGCTATCTACAAATGAACAA CTTGAAAACCTGAGGACACTGCCGTGTAATCTGTGTGAGACATGGAACTTCGGTAATAGCTACT TATCCTGTGGGCTTACTGGGGCCCAAGGACTCTGCTCAACCTCTCCTCAGTGGTGGTGTCT GGCGGGGGGGCTCCGGTGGTGGTGGTCTGTGAGCTCTGTGACTCAGGAACCTTCACCTACCGT ATCACCTGGTGAACAGTCACTCACTTGTGCTCCTCGACTGGGCTGTACATCTGGCTACT ACCCAACTGGTCCAAACAAACAGGTCAGGCAACCCGCTGCTAATAGTGCCACTGACATG AGGCCCTGTGTAATCTCTGCCAGATCTCAGGCTCCCTGCTGGAGGCAAGCTGCCCTCACCT CTCAGGGTACAGCCAGAGATGAGGCAAGATTAATGTGTCTATGTGTACAGCAACCCGCTGGG TGTTGGTGGAGAACCAAACTGACTGTCTA</p>
	99.	CDR-L1 of E1L	artificial	aa		GSSTGAVTSGYYPN
	100.	CDR-L2 of E1L	artificial	aa		GTKFLAP
	101.	CDR-L3 of E1L	artificial	aa		ALWYSNRWV
	102.	CDR-H1 of E1L	artificial	aa		KYAMN
	103.	CDR-H2 of E1L	artificial	aa		RIRSKYNNYATYYADSVKS
	104.	CDR-H3 of E1L	artificial	aa		HGNFGNSYTSYYAY
	105.	VH of E1L	artificial	aa		EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYYADS VKSRFTISRDDSKNTAYLQMNLLKTEDTAVYYCVRHGNFGNSYTSYYAYWGQGILVTVSS
	106.	VH of E1L	artificial	nt		<p>GAGTGCAGCTGGTCTGAGTCTGGAGGAGGATTGGTCAGCCTGGAGGTCATTGAACTCTCATG TGCAGCCTCTGGATTACCTTCAATAAGTACGCCATGAATGGTCCGCCAGGCTCCAGGAAAGG GTTTGGAAATGGGTGCTCGCATAGAAGTAAATATAATAATATGCAACATATTATGCCGATTCA GTGAAATCGAGGTTCAACATCTCCAGAGATGATTCAAAAACAACCTGCCCTATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTACTGTGTGAGACATGGGAACCTCGGTAATAGCTACA CATCCTACTACGCTTACTGGGGCCCAAGGACTCTGCTCACCGTCTCCTCA</p>
	107.	VL of E1L	artificial	aa		<p>QTVVTQEPSTLVSPGGTVTLTCGSSTGAVTSGYYPNWVQKPGQAPRGLIGGTFKFLAPGTPARFS GSLLGKKAALTLSGVQPEDEAEYCALWYSNRWVFGGTCLTLV</p>
	108.	VL of E1L	artificial	nt		<p>CAGACTGTGTGACTCAGGAACCTTCACTCACCGTATCACTGGTGGAAACAGTCACACTCACTTG TGGTCTCTCGACTGGGCTGTACATCTGGCTACTACCAAACTGGTCCAAACAAACAGGTC AGGCACCCCGTGGTCTAATAGTGGGACTAAGTCTCGCCCCGGTACTCCTGCCAGATTCTCA GGCTCCCTGCTTGGAGGCAAGGTCGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGA ATATTACTGTGCTCTATGTTACAGCAACCGCTGGGTGTTCTGGTGGAGGAACCAACTGACTGTCC TA</p>
	109.	VH-P of E1L	artificial	aa		EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYYADS VKSRFTISRDDSKNTAYLQMNLLKTEDTAVYYCVRHGNFGNSYTSYYAYWGQGILVTVSS
	110.	VH-P of E1L	artificial	nt		GAGTGCAGCTGCTCGAGTCTGGAGGAGGATTGGTGCAGCCTGGAGGTCATTGAACTCTCATG TGCAGCCTCTGGATTACCTTCAATAAGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG

					<p>GTTTGAATGGGTGCTCGCATAAGAAGTAATAATAATATGCAACATATTATGCCGATTCA GTGAAATCGAGGTTACCATCTCCAGAGATGATCAAAAAACACTGCCTATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTACTGTGTGAGACATGGAACTTCGGTAATAGCTACA CATCTACTACGCTTACTGGGGCCCAAGGACTGCTGCTCACCTCTCCTCA</p>
111.	VL-P of E1L	artificial	aa		<p>ELVVTQPSLTVSPGGTVTLTCSSTGAVTSYYPNWNVQKPGQAPRGLIGGKFLAPGPAPFS CSLLGGKAAALTLGVPQPEDEAEYICALWYSNRWVFGGKLTIVL</p>
112.	VL-P of E1L	artificial	nt		<p>GAGCTCGTTGTGACTCAGGAACCTTCACTACCGTATCACTGGTGAACAGTCACACTCACTTG TGGCTCCTCGACTGGGCTGTACATCTGCTACTACCCAAACTGGTCCAAACAAACAGGTC AGCACCCCGTGGTCTAATAGGTGGACTAGTCTCTGCCCCCGTACTCCTGCCAGATTCTCA GGCTCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGA ATATTACTGTGCTCTATGTTACAGCAACCGCTGGGTGTTCCGTGGAGGAACCAACTGACTGCTC TA</p>
113.	VH-VL of E1L	artificial	aa		<p>EVQLVESGGGLVQPGSLKLSCAASGFTTNKYAMNWNVQAPGKLEWVARI RSKYNNYATYYADS VKSRFTISRDDSKNTAYLQMNLLKTEDTAVYCVRHGNGFNSYTSYAYWGQGLTVTVSSGGGGS GGGSGGGGSGTVVTQEPSTVSPGGTVTLTCSSTGAVTSYYPNWNVQKPGQAPRGLIGGKTF LAPGTPARFSGSLGGKAAALTLGVPQPEDEAEYICALWYSNRWVFGGKLTIVL</p>
114.	VH-VL of E1L	artificial	nt		<p>GAGGTGCAGCTGGTCGAGTCTGGAGGAGGATGGTGCAGCCTGGAGGGTCACTTGAACCTCTCATG TGCAGCCTCTGGATTACCTTCAATAAGTACGCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAAGAAGTAATAATAATAATATGCAACATATTATGCCGATTCA GTGAAATCGAGGTTACCATCTCCAGAGATGATCAAAAAACACTGCCTATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTCTGTGTGAGACATGGAACTTCGGTATAGCTACA CATCTACTACGTTACTGGGGCCAGGACTCTGGTCACTGCTCCTCAGGTGGTGGTGGTCTT GGCGCGGGGCTCCGGTGGTGGTCTCAGACTGTTGACTCAGGAACCTTCACTCACCGT ATCACCTGGTGAACAGTCACACTCACTTGTGGTCTCTCGACTGGGCTGTTACATCTGGCTACT ACCCAAACTGGTCCCAACAAACCCAGGTCAGGCACCCCGTGGTCTAATAGGTGGGACTAAGTTC CTCGCCCCCGTACTCCTGCCAGATTCTCAGGCTCCCTGCTTGGAGGCAAGGCTGCCCTCACCT CTCAGGGGTACAGCCAGAGATGAGGAGATAATATTACTGTGCTCTATGGTACAGCAACCGCTGGG TGTTCCGTGGAGGAACCAACTGACTGCTCTA</p>
115.	VH-VL-P of E1L	artificial	aa		<p>EVQLVESGGGLVQPGSLKLSCAASGFTTNKYAMNWNVQAPGKLEWVARI RSKYNNYATYYADS VKSRFTISRDDSKNTAYLQMNLLKTEDTAVYCVRHGNGFNSYTSYAYWGQGLTVTVSSGGGGS GGGSGGGGSELVVTQEPSTVSPGGTVTLTCSSTGAVTSYYPNWNVQKPGQAPRGLIGGKTF LAPGTPARFSGSLGGKAAALTLGVPQPEDEAEYICALWYSNRWVFGGKLTIVL</p>
116.	VH-VL-P of E1L	artificial	nt		<p>GAGTGCAGCTCTCCACTCTCCAGGAGGATGGTCCACCTCGACGCTCATTCACAACTCTCATC TGACGCTCTGGATTACCTTCAATAAGTACGCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAAGAAGTAATAATAATAATATGCAACATATTATGCCGATTCA GTGAAATCGAGGTTACCATCTCCAGAGATGATCAAAAAACACTGCCTATCTACAAATGAACAA CTTCAAAACTGAGGACACTGCCGTGTACTACTGTGTGAGACATGGAACTTCGGTATAGCTACA</p>

				CATCCTACTAGCCTTACTGGGGCCAAGGACICTGGTCAACGCTCTCCTCAGGTGGTGGTCTCT GGCGGGCGGCTCCGGTGGTGGTCTGAGTCGTTGACTCAGGAACCTTCACTCACCGT ATCACCTGGTGAACAGTCACTCACTTGTGGCTCTGAGTGGGCTGTACATCTGGCTACT ACCCAACTGGTCCAAACAAACCAGGTCAAGCAACCCGCTGGTCTAATAGTGGGACTAAGTTC CTGCCCCCGGTACTCTCCAGATTCTCAGGCTCCCTGCTGGAGGCAAGGCTGCCCTCACCT CTCAGGGGTACAGCAGAGGATGAGGCAGAAATATTACTGCTCTATGGTACAGCAACCGTGGG TGTCGGTGGAGGAACAACTGACTGCTCTA
117.	CDR-L1 of E2M	artificial	aa	RSSTGAVTSGYYPN
118.	CDR-L2 of E2M	artificial	aa	ATDMRPS
119.	CDR-L3 of E2M	artificial	aa	ALWYSNRWV
120.	CDR-H1 of E2M	artificial	aa	GYAMN
121.	CDR-H2 of E2M	artificial	aa	RIRSKYNNYATYYADSVKE
122.	CDR-H3 of E2M	artificial	aa	HRNFGNSYLSWFAY
123.	VH of E2M	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAASGFTFNGYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADS VKERFTISRDDSKNTAYLQMNLLKTEDTAVYYCVHRHFNFGNSYLSWFAYWGQGLVTVSS
124.	VH of E2M	artificial	nt	GAGGTGCAGCTGGTCGAGTCTGGAGGAGGATTGGTGACGCTGGAGGGTCAITGAACTCTCATG TGCAGCCTCTGGATTCACTTCAATGGCTACGCCATCAATTAATAATATGCAACATATTATGCGGATTCA GTTTGAATGGGTGCTCGCATAGAAGTAAATATAATATGCAACATATTATGCGGATTCA GTGAAAGAGAGGTTCAACATCTCCAGAGATGATTCAAAAACATAGCCTATCTACAATGAACAA CTTGAAACTGAGGACACTGCCGTGACTACTGTGAGACATAGGAACCTCGGTAATAGCTACT TATCCTGGTTCGCTTACTGGGGCAAGGACTCTGGTCACCGTCTCTCTCA
125.	VL of E2M	artificial	aa	QTVVTQEPSTLVSPGTVTLTCRSSTGAVTSGYYPNWVQKPGQAPRGLIGATDMRPSGTPAREF GSLGGKAALILSGVQPEDEAEYYCALWYSNRWVFGGTKLTVL
126.	VL of E2M	artificial	nt	CAGACTGTTGTGACTCAGGAACCTTCACTCACCGTATCACCTGGTGAACAGTCACACTCACTTG TCGCTCCTCGACTGGGCTGTACATCTGGCTACTACCAAACTGGGTCCAACAAAACAGGTC AGCACCCCGTGGTCTAATAGGTGCCACTGACATAGGCCCTCTGGTACTCCTGCCAGATTCTCA GGCTCCCTGCTTGGAGGCAAGGTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGA ATATTACTGTGCTCTATGGTACAGCAACCGCTGGGTGCTGGTGGAGAACCACTGACTGTCC TA
127.	VH-P of E2M	artificial	aa	EVQLLESGLLVQPGGSLKLSCAASGFTFNGYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADS VKERFTISRDDSKNTAYLQMNLLKTEDTAVYYCVHRHFNFGNSYLSWFAYWGQGLVTVSS
128.	VH-P of E2M	artificial	nt	GAGGTGCAGCTGCTCGAGTCTGGAGGAGGATTGGTGACGCTGGAGGGTCAITGAACTCTCATG TGCAGCCTCTGGATTCACTTCAATGGCTACGCCATCAACTGAGTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAAATATAATATGCAACATATTATGCGGATTCA GTGAAAGAGAGGTTCAACATCTCCAGAGATGATTCAAAAACATAGCCTATCTACAATGAACAA CTTGAAAACTGAGGACACTGCCGTGACTACTGTGAGACATAGGAACCTCGGTAATAGCTACT

129.	VL-P of E2M	artificial	aa	TATCCTGGTTCGCTTACTGGGGCAAGGACCTCTGGTCACCGTCTCCTCA ELVVTQEPSLTVSPGGTTLTCSRSTGAVTSGYYPNWVQKPGQAPRGLIGATDMRPSGTPARFS GSLGGKAAATLSGVQPEDEAEYICALWYSNRWVFGGKLTIVL
130.	VL-P of E2M	artificial	nt	GAGCTCGTTGTGACTCAGGAACCTTCACTCACCGTATCACCTGGTGAACAGTCACACTCACTTG TCGCTCTCGACTGGGCTGTACATCTGGCTACTACCCAACTGGTCCAAACAAACCAGGTC AGGCACCCCGTGGTCTAATAGGTGCCACTGACATGAGGCCCTCTGGTACTCCTGCCAGATTCTCA GGCTCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATCAGGCAGA ATATTACTGTGCTCTATGTTACAGCAACCGCTGGGTGTTGGTGGAGGAACCAAACTGACTGTCC TA
131.	VH-VL of E2M	artificial	aa	EVQIVESGGGLVQPGSLKLSCAASGFTFNGYAMNWNVRQAPGKLEWVARIRSKYNNYATYYADS VKERFTISRDDSKNTAYLQMNILKTEDTAVYCVHRNFGNSYLSWFAYWQGTLTVTVSSGGGGS GGGSGGGGSGTWTQEPSTLVSPGGTVILTCRSSSTGAVTSGYYPNWVQKPGQAPRGLIGATDM RPSGTPARFSGSLGGKAAATLSGVQPEDEAEYICALWYSNRWVFGGKLTIVL
132.	VH-VL of E2M	artificial	nt	GAGTGCAGCTGTCGAGTCTGGAGGAGGATGGTGCAGCCTGGAGGTCATTGAAACTCTCATG TGACGCTCTGGATTCACTTCAATGGCTACGCCATGAACCTGGTCCGCCAGGTCACAGGAAAGG GTTTGAATGGGTTGCTCGCATAGAAGTAATAATAATATATGCAACATATATGCCCATTCA GTGAAGAGAGGTTTACCATTCCAGAGATGATCAAAAACACTGCCTATCTACAAATGAACAA CTTGAAACTGAGGACACTGCCGTGTACTGTGTGAGACATAGGAACCTCGGTAACTAGCTACT TATCCTGTTTCGTTACTGGGGCCAAAGGACTCTGGTCAACCTCTCCTCAGTGGTGGTGTCTT GGCGCGCGGCTCCGGTGGTGGTCTCAGACTGTGTGACTCAGGAACCTTCACTCACCGT ATCACTGGTGGAAACAGTCACACTCCTGCTGCTCCTCGACTGGGCTGTACATCTGGCTACT ACCCAACTGGGTCCAAACAAACAGGTCAGGACCCCGTGGTCTAATAGGTGCCACTGACATG AGGCTCTGTTACTCCTGCCAGATTCTCAGGCTCCTGCTTGAGGCAAGGTCGCCCTCACCT CTCAGGGGTACAGCCAGAGGATGAGGCAGATAATTAATGTGTCTATGTTACAGCAACCGCTGGG TGTTGGTGGAGGAACCAACTGACTGCTCTA
133.	VH-VL-P of E2M	artificial	aa	EVOLLESGGGLVQPGSLKLSCAASGFTFNGYAMNWNVRQAPGKLEWVARIRSKYNNYATYYADS VKERFTISRDDSKNTAYLQMNILKTEDTAVYCVHRNFGNSYLSWFAYWQGTLTVTVSSGGGGS GGGSGGGGSEIVTQEPSTLVSPGGTVILTCRSSSTGAVTSGYYPNWVQKPGQAPRGLIGATDM RPSGTPARFSGSLGGKAAATLSGVQPEDEAEYICALWYSNRWVFGGKLTIVL
134.	VH-VL-P of E2M	artificial	nt	GAGTGCAGCTGTCGAGTCTGGAGGAGGATGGTGCAGCCTGGAGGTCATTGAAACTCTCATG TGACGCTCTGGATTCACTTCAATGGCTACGCCATGAACCTGGTCCGCCAGGTCACAGGAAAGG GTTTGAATGGGTTGCTCGCATAGAAGTAATAATAATATGCAACATATATGCCGATTCA GTGAACACAGGTTTACCATTCCACAGATGATCAAAAACACTGCCCTATCTACAAATGAACAA CTTGAAACTGAGGACACTGCCGTGTACTGTGTGAGACATAGGAACCTCGGTAACTAGCTACT TATCCTGGTTCGTTACTGGGGCCAAAGGACTCTGGTCAACCTCTCCTCAGTGGTGGTGGTCT GGCGGCGCGGCTCCGGTGGTGGTCTGAGCTCGTTGACTCAGGAACCTTCACTCACCGT ATCACCTGGTGAACAGTCACACTCCTGCTGCTCCTGACTGGGCTGTATACATCTGGCTACT

					ACCAAACTGGGTCCAAACAAAAACAGGTGAGGCACCCCGTGGTCTAATAGGTGCCACTGACATG AGGCCCTCTGGTACTCCTGCCAGATTCTCAGGTCCTCCTGGAGCAAGGCTGCCCTCACCT CTCAGGGGTACAGCCAGGATGAGGCAGAAATATTACTGTGCTCTATGGTACAGCAACCGGTGGG TGTTGGTGGAGGAACCAAACTGACTGTCTTA
135.	CDR-L1 of F7O	artificial	aa		GSSTGAVTSGYYPN
136.	CDR-L2 of F7O	artificial	aa		GTKFLAP
137.	CDR-L3 of F7O	artificial	aa		ALMYSNRWV
138.	CDR-H1 of F7O	artificial	aa		VYAMN
139.	CDR-H2 of F7O	artificial	aa		RIRSKYNNYATYYADSVKK
140.	CDR-H3 of F7O	artificial	aa		HGNFGNSYISWWAY
141.	VH of F7O	artificial	aa		EVQLVESGGGLVQPGGSLKLSAASGFTFENVYAMNWRQAPGKGLEWVARIRSKYNNYATYYADS VKRFTISRDDSKNTAYLQMNLLKTEDTAVYCVRHGNGNSYISWWAYWGQGLTVVSS
142.	VH of F7O	artificial	nt		GAGTGCAGCTGGTCGAGTCTGGAGGAGGATTGGTCAGCCTGGAGGTCATTGAAACTCTCATG TGCAGCCTCTGGATTACCTTCAATGTGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGTTGCTCGCATAGAAGTAATAATAATATGCAACATATTATGCCGATTCA GTGAAAAAGAGGTTACCATCTCCAGAGATGATCAAAAAACACTGCCTATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTACTGTGTGAGACATGGAACTTCGGTATAGCTACA TATCTGTGGGCTTACTGGGCCAAGGACTGTGTCACCGTCTCTCTCA
143.	VL of F7O	artificial	aa		QTVVTEPSLTVPGGTVTLTCGSSTGAVTSGYYPNWRQAPRGLIGGTKFLAPGTPARFS GSLLGKAAALTLSGVQPEDEAEYICALWYSNRWVFGGTKLTVL
144.	VL of F7O	artificial	nt		CAGACTGTTGTGACTCAGGAACCTTCACTACCTGATCACCTGGTGGAAACAGTCACACTACTTG TGGCTCCTCGACTGGGCTGTACATCTGGCTACTACCCAAACTGGGTCCAAACAAACAGGTC AGGCACCCCGTGGTCTAATAGGTGGACTAAGTCTCGCCCCCGTACTCCTGCCAGATTCTCA GGCTCCCTGTGGAGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGA ATATTACTGTGCTCTATGGTACAGCAACCGCTGGGTGCTGCTGGAGGAACCAAACTGACTGCC TA
145.	VH-P of F7O	artificial	aa		EVQLLESGLLVQPGGSLKLSAASGFTFENVYAMNWRQAPGKGLEWVARIRSKYNNYATYYADS VKRFTISRDDSKNTAYLQMNLLKTEDTAVYCVRHGNGNSYISWWAYWGQGLTVVSS
146.	VH-P of F7O	artificial	nt		GAGTGCAGCTGCTCGAGTCTGGAGGAGGATTGGTCAGCCTGGAGGTCATTGAAACTCTCATG TGACGCTCTGGATTACCTTCAATGTGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGTTGCTCGCATAGAAGTAATAATAATATGCAACATATTATGCCGATTCA GTGAAAAAGAGGTTACCATCTCCAGAGATGATCAAAAAACACTGCCTATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTACTGTGTGAGACATGGAACTTCGGTATAGCTACA TATCCTGGTGGGCTTACTGGGCCAAGGACTCTGGTCACCGTCTCTCTCA
147.	VL-P of F7O	artificial	aa		ELVVTEPSLTVPGGTVTLTCGSSTGAVTSGYYPNWRQAPRGLIGGTKFLAPGTPARFS GSLLGKAAALTLSGVQPEDEAEYICALWYSNRWVFGGTKLTVL

148.	VL-P of F70	artificial	nt	GAGCTCGTGTGACTCAGGAACCTTCACTACCGTATCACCTGGTGGAAACAGTCACACTCACTTG TGGCTCTCGACTGGGCTGTACATCTGGCTACTACCAAACTGGTCCAAACAAAACAGGTC AGCACCCCGTGGTCTAATAGGTGGGACTAAGTCTCCGCCCGGCTACTCCTGCCAGATTCTCA GGTCCCTGCTTGGAGGCAAGGTGCCCTCACCTCTCAGGGGTACAGCCAGGATGAGGCAGA ATATTACTGTGCTCTATGGTACAGCAACCGCTGGGTGTCGGTGGAGGAACCAAACTGACTGTCC TA
149.	VH-VL of F70	artificial	aa	EVQLVESGGGLVQPGGSLKLSCAASGFTFNVYAMNWRQAPGKGLEWVARIRSKYNNYATYYADS VKRRFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFGNSYISWWAYWGQGLTVTVSSGGGGS GGGSGGGGSQTWVTOEPSLTVSPGGTVLTCGSSTGAVTSGYYPNWVQKPGQAPRGLIGGTFK LAPGTPARFSGSLGGKAALTLGVQPEDEAEYICALWYSNRWVFGGKLTVL
150.	VH-VL of F70	artificial	nt	GAGTGCAGCTGGTCGAGTCTGGAGGAGGATGGTGCAGCTGGAGGGTCATTGAAACTCTCATG TGCAGCTCTGGATTCACTTCAATGTGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAAATATAATATATGCAACATATTATGCCGATTCA GTGAAAAAGAGGTTACCATCTCCAGAGATGATTCAAAAACACTGCCTATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTGTGTGAGACATGGAACTTCGGTAATAGCTACA TATCCTGGTGGGCTTACTGGGCCAAGGACTCTGGTCACCGTCTCCTCAGGTGGTGGTCTCT GGCGGGCGGCTCCGGTGGTGGTTCACAGCTGTGTGACTCAGGAACCTTCACTCACCGT ATCAGCTGGTGGAACAGTCACTCACTTGTGGTCTCGACTGGGCTGTACATCTGGCTACT ACCCAACTGGTCCAAACAAAACAGGTCAGCACCCCGTGGTCTAATAGTGGGACTAAGTTC CTCGCCCCGGTACTCTCGCCAGATTCTCAGGCTCCCTGCTGGAGGCAAGGCTGCCCTCACCT CTCAGGGGTACAGCCAGAGGATGAGGCAGATATTACTGTGCTCTATGGTACAGCAACCGCTGGG TGTTCCGTGGAGAACCAACTGACTGTCTTA
151.	VH-VL-P of F70	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAASGFTFNVYAMNWRQAPGKGLEWVARIRSKYNNYATYYADS VKRRFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFGNSYISWWAYWGQGLTVTVSSGGGGS GGGSGGGGSELVVTQEPSLTVSPGGTVLTCGSSTGAVTSGYYPNWVQKPGQAPRGLIGGTFK LAPGTPARFSGSLGGKAALTLGVQPEDEAEYICALWYSNRWVFGGKLTVL
152.	VH-VL-P of F70	artificial	nt	GAGTGCAGCTGCTCGAGTCTGGAGGAGGATGGTGCAGCTGGAGGGTCATTGAAACTCTCATG TGCAGCTCTGGATTCACTTCAATGTGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAAATATAATATATGCAACATATTATGCCGATTCA GTGAAAAAGAGGTTACCATCTCCAGAGATGATTCAAAAACACTGCCTATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTGTGTGAGACATGGAACTTCGGTAATAGCTACA TATCCTGGTGGGCTTACTGGGCCAAGGACTCTGGTCACCGTCTCCTCAGGTGGTGGTCTCT GGCGGGCGGCTCCGGTGGTGGTTCAGCTGTGTGACTCAGGAACCTTCACTCACCGT ATCAGCTGGTGGAACAGTCACTCACTTGTGGTCTCGACTGGGCTGTACATCTGGCTACT ACCCAACTGGTCCAAACAAAACAGGTCAGGCACCCCGTGGTCTAATAGTGGGACTAAGTTC CTCGCCCCGGTACTCTCGCCAGATTCTCAGGCTCCCTGCTGGAGGCAAGGCTGCCCTCACCT CTCAGGGGTACAGCCAGAGGATGAGGCAGATATTACTGTGCTCTATGGTACAGCAACCGCTGGG

153.	CDR-L1 of F12Q	artificial	aa	TGTTGGTGGAGGAACCAAACTGACTGTCTTA
154.	CDR-L2 of F12Q	artificial	aa	GSSTGAVTSGNYPN
155.	CDR-L3 of F12Q	artificial	aa	GTKFLAP
156.	CDR-H1 of F12Q	artificial	aa	VLWYSNRWV
157.	CDR-H2 of F12Q	artificial	aa	SYAMN
158.	CDR-H3 of F12Q	artificial	aa	RIRSKYNNYATYYADSVKG
159.	VH of F12Q	artificial	aa	HGNEGNSYVSWWAY
160.	VH of F12Q	artificial	nt	EVQLVDSGGGLVQPGGSLKLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADS VKGRFTISRDDSKNTAYLQMNLLKTEDTAVYYCVRHGNGNSYVSWWAYWGQGLTVTVSS GAGTGCAGCTGGTCTGAGTCTGGAGGAGGATGGTGCAGCCTGGAGGTCATTGAAACTCTCATG TGCAGCCTCTGGATTACCTTCAATAGCTAGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAATAATAATATATGCAACATATATGCCGATTCA GTGAAAGGCAGGTTACCATCTCCAGAGATGATCAAAAAACACTGCCTATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTGTGTGAGACATGGGAACCTTCGGTAATAGCTACG TTTCTCTGGTGGCTTACTGGGGCCAAAGGACTCTGGTCACTCTCTCTCA
161.	VL of F12Q	artificial	aa	QTVVTQEPSLTVSPGGTVTLTSGSSTGAVTSGNYPNWVQKPGQAPRGLIGGKFLAPGTPARFS GSLLGKAAITLSGVQPEDEAEYYCVLWYSNRWVFGGKLTIVL
162.	VL of F12Q	artificial	nt	CAGACTGTTGTGACTCAGGAACCTTCACTCACCGTATCACCTGGTGGAAACAGTCACACTCTTG TGGCTCCTCGACTGGGCTGTACATCTGGCAACTACCCAACTGGTGGTCCAAAAACAGGTC AGGACCCCGTGGTCTAATAGGTGGACTAAGTCTCGCCCGGTACTCTCTGCCGATTCTCA GGTCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGA ATATTACTGTGTTCTATGGTACAGCAACCGCTGGGTGTTCTGGTGGAGGAACCAAACTGACTGTCC TA
163.	VH-P of F12Q	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADS VKGRFTISRDDSKNTAYLQMNLLKTEDTAVYYCVRHGNGNSYVSWWAYWGQGLTVTVSS
164.	VH-P of F12Q	artificial	nt	GAGGTGCAGCTGCTCGAGTCTGGAGGAGGATTTGTCAGCCTGGAGGGTCAITGAAACCTCTCATG TGCAGCCTCTGGATTACCTTCAATAGCTAGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAATAATAATATATGCAACATATATGCCGATTCA GTGAAAGGCAGGTTACCATCTCCAGAGATGATCAAAAAACACTGCCTATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTGTGTGAGACATGGGAACCTTCGGTAATAGCTACG TTTCTCTGGTGGCTTACTGGGGCCAAAGGACTCTGGTCACTCTCTCTCA
165.	VL-P of F12Q	artificial	aa	ELVVTQEPSLTVSPGGTVTLTSGSSTGAVTSGNYPNWVQKPGQAPRGLIGGKFLAPGTPARFS GSLLGKAAITLSGVQPEDEAEYYCVLWYSNRWVFGGKLTIVL
166.	VL-P of F12Q	artificial	nt	GAGCTCGTGTGACTCAGGAACCTTCACTCACCGTATCACCTGGTGGAAACAGTCACACTCACTTG TGGCTCCTCGACTGGGCTGTACATCTGGCAACTACCCAACTGGTGGTCCAAAAACAGGTC AGGACCCCGTGGTCTAATAGGTGGGACTAAGTCTCTCGCCCGGTACTCTCTGCCGATTCTCA

167.	VH-VL of F12Q	artificial	aa	GGCTCCCTGCTTGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGA ATATTACTGTGTTCTATGGTACAGCAACCGCTGGGTGTTCCGTGGAGGAACCAAACTGACTGTCC TA
168.	VH-VL of F12Q	artificial	nt	EVQLVESGGGLVQPGGSLKLSKAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADS VKGRFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFNSYVSWWAYWGQGLVTVSSSGGGS GGCGSGGGSQTVVTQEPSTLTVSPGGTVTLTCSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFK LAPGTPARFSGSLGGKAALTLGSGVQPEDEAEYCYVLWYSNRWVFGGKLTIVL GAGGTGACGCTGGTCGAGTCTGGAGGAGGATGGTGCAGCCTGGAGGGTCATTGAAACTCTCATG TGCAGCCTCTGGATTACCTTCAATAGCTAGCATGCACTGGTCCGCCAGGCTCCAGGAAAGG GTTTGGAATGGGTGCTCGCATAGAAGTAATAATAATAATAATAATATGCAACATATTATGCCGATTCA GTGAAAGGCAGGTTACCATCTCCAGAGATGATTCAAAAACAACCTGCCTATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTACTGTGTGAGACATGGAACTTCGGTAATAGCTACG TTTCTGCTGGCTTACTGGGGCCAGGGACTCTGGTACCGTCTCCTCAGGTGGTGGTGGTCT GGCGCGCGGCTCCGGTGGTGGTCTCAGACTGTTGTGACTCAGGAACCTTCACTCACCCT ATCACCTGGTGAACAGTCACACTCCTTGTGGCTCCTCGACTGGGCTGTTACATCTGCAACT ACCCAAACTGGGTCCAAACAAACCCAGGTACAGGCACCCCGTGGTCTAATAGGTGGGACTAAGTTC CTCGCCCCGGTACTCCTGCCAGATTCTCAGGCTCCTGCTTGAGGCAAGGCTGCCCTCACCT CTCAGGGGTACAGCCAGAGGATGAGGCAATAATACTGTGTTCTATGGTACAGCAACCGCTGGG TGTCGGTGGAGAACCAAACTGACTGTCTTA
169.	VH-VL-P of F12Q	artificial	aa	EVQLVESGGGLVQPGGSLKLSKAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADS VKGRFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFNSYVSWWAYWGQGLVTVSSSGGGS GGCGSGGGSSELVVTQEPSTLTVSPGGTVTLTCSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFK LAPGTPARFSGSLGGKAALTLGSGVQPEDEAEYCYVLWYSNRWVFGGKLTIVL GAGGTGACGCTGCTCGAGTCTGGAGGAGGATGGTGCAGCCTGGAGGGTCATTGAAACTCTCATG TGCAGCCTCTGGATTACCTTCAATAGCTACGCATGAACTGGTCCGCCAGGCTCCAGGAAAGG GTTTGGAATGGGTGCTCGCATAGAAGTAATAATAATAATAATAATATGCAACATATTATGCCGATTCA GTGAAAGGCAGGTTACCATCTCCAGAGATGATTCAAAAACAACCTGCCTATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTACTGTGTGAGACATGGAACTTCGGTAATAGCTACG TTTCTGCTGGCTTACTGGGGCCAGGGACTCTGGTACCGTCTCCTCAGGTGGTGGTGGTCT GGCGCGCGGCTCCGGTGGTGGTCTCAGACTGTTGTGACTCAGGAACCTTCACTCACCCT ATCACCTGGTGAACAGTCACACTCCTTGTGGCTCCTCGACTGGGCTGTTACATCTGCAACT ACCCAAACTGGGTCCAAACAAACCCAGGTACAGGCACCCCGTGGTCTAATAGGTGGGACTAAGTTC CTCGCCCCGGTACTCCTGCCAGATTCTCAGGCTCCTGCTTGAGGCAAGGCTGCCCTCACCT CTCAGGGGTACAGCCAGAGGATGAGGCAATAATACTGTGTTCTATGGTACAGCAACCGCTGGG TGTCGGTGGAGAACCAAACTGACTGTCTTA
170.	VH-VL-P of F12Q	artificial	nt	EVQLVESGGGLVQPGGSLKLSKAASGFTFNSYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADS VKGRFTISRDDSKNTAYLQMNNLKTEDTAVYCVRHGNFNSYVSWWAYWGQGLVTVSSSGGGS GGCGSGGGSSELVVTQEPSTLTVSPGGTVTLTCSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFK LAPGTPARFSGSLGGKAALTLGSGVQPEDEAEYCYVLWYSNRWVFGGKLTIVL GAGGTGACGCTGCTCGAGTCTGGAGGAGGATGGTGCAGCCTGGAGGGTCATTGAAACTCTCATG TGCAGCCTCTGGATTACCTTCAATAGCTACGCATGAACTGGTCCGCCAGGCTCCAGGAAAGG GTTTGGAATGGGTGCTCGCATAGAAGTAATAATAATAATAATAATATGCAACATATTATGCCGATTCA GTGAAAGGCAGGTTACCATCTCCAGAGATGATTCAAAAACAACCTGCCTATCTACAAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTACTGTGTGAGACATGGAACTTCGGTAATAGCTACG TTTCTGCTGGCTTACTGGGGCCAGGGACTCTGGTACCGTCTCCTCAGGTGGTGGTGGTCT GGCGCGCGGCTCCGGTGGTGGTCTCAGACTGTTGTGACTCAGGAACCTTCACTCACCCT ATCACCTGGTGAACAGTCACACTCCTTGTGGCTCCTCGACTGGGCTGTTACATCTGCAACT ACCCAAACTGGGTCCAAACAAACCCAGGTACAGGCACCCCGTGGTCTAATAGGTGGGACTAAGTTC CTCGCCCCGGTACTCCTGCCAGATTCTCAGGCTCCTGCTTGAGGCAAGGCTGCCCTCACCT CTCAGGGGTACAGCCAGAGGATGAGGCAATAATACTGTGTTCTATGGTACAGCAACCGCTGGG TGTCGGTGGAGAACCAAACTGACTGTCTTA
171.	CDR-L1 of I2C	artificial	aa	GSSTGAVTSGNYPN
172.	CDR-L2 of I2C	artificial	aa	GTKFLAP

173.	CDR-L3 of I2C	artificial	aa	VLWYSNRWV
174.	CDR-H1 of I2C	artificial	aa	KYAMN
175.	CDR-H2 of I2C	artificial	aa	RIRSKYNNYATYYADSVKD
176.	CDR-H3 of I2C	artificial	aa	HGNFGNSYISYWAY
177.	VH of I2C	artificial	aa	EVQLVESGGGLVQPGGSLKLSKAASGFTFNKYAMNWVRQAPKGLWVARIRSKYNNYATYYADS VKDRFTISRDDSKNTAYLQMNLIKTEDTAVYYCVRHGNGNSYISYWAYWGQGLVTVSS
178.	VH of I2C	artificial	nt	GAGGTGCAGCTGGTCTGAGTCTGGAGGAGGATTGGTGGAGCTGGAGGGTCA"TTGAAACTCTCATG TGCAGCCTCTGGATTCACTTCAATAAGTACGCCATGAACCTGGTCCGAGGCTCCAGGAAAGG GTTTGGAATGGGTGCTCGCATAAGAAGTAAATATAATAATTATGCAACATATTATGCCGATTCA GTGAAAGACAGGTTACACATCTCCAGAGATGATTCAAAAAACACTGCCTATCTACAATGAACAA CTTGAAAACCTGAGGACACTGCCGTGTACTACTGTGAGACATGGAACTTCGGTAATAGCTACA TATCCTACTGGGCTTACTGGGGCCAAGGACTCTGGTCAACCTCTCCTCA
179.	VL of I2C	artificial	aa	QTVVTQEPSLTVSPGGTVTLTSGSSTGAVTSGNYPNWVQKPGQAPRGLIGGTKFLAPGTPARFS GSLGGKAALILSGVQPEDEAEYYCVLWYSNRWVFGGTKLTVL
180.	VL of I2C	artificial	nt	CAGACTGTTGTGACTCAGGAACCTTCACTCACTCACTCACTCACTGGTGGACAGTCACACTCACTTG TGGCTCCTCGACTGGGCTGTACATCTGGCACTACCCAACTGGGTCCACAAAAACCCAGGTC AGGCACCCCGGTGCTTAATAGTGGGACTAAGTCTCTGCCCCGGTACTCTCTGCCAGATTCTCA GGCTCCCTGCTTGAGGCAAGGCTGCCCTCACTCCTCAGGGGTACAGCCAGAGGATGAGGCAGA ATATTACTGTGTTCTATGGTACAGCAACCGCTGGGTGGTGGAGAACCAACTGACTGTCC TA
181.	VH-P of I2C	artificial	aa	EVQLLESGLLVQPGGSLKLSKAASGFTFNKYAMNWVRQAPKGLWVARIRSKYNNYATYYADS VKDRFTISRDDSKNTAYLQMNLIKTEDTAVYYCVRHGNGNSYISYWAYWGQGLVTVSS
182.	VH-P of I2C	artificial	nt	GAGGTGCAGCTGCTGAGTCTGGAGGAGGATTGGTGCAGCCTGGTCCGAGGCTCATTTGAACCTCTCATG TGCAGCCTCTGGATTCACTTCAATAAGTACGCCATGAACCTGGTCCGAGGCTCCAGGAAAGG GTTTGGAATGGGTGCTCGCATAAGAAGTAAATATAATAATTATGCAACATATTATGCCGATTCA GTGAAAGACAGGTTACACATCTCCAGAGATGATTCAAAAAACACTGCCTATCTACAATGAACAA CTTGAAAACCTGAGGACACTGCCGTGTACTACTGTGTGAGACATGGAACTTCGGTAATAGCTACA TATCCTACTGGGCTTACTGGGGCCAAGGACTCTGGTCAACCTCTCCTCA
183.	VL-P of I2C	artificial	aa	ELVVTQEPSLTVSPGGTVTLTSGSSTGAVTSGNYPNWVQKPGQAPRGLIGGTKFLAPGTPARFS GSLGGKAALILSGVQPEDEAEYYCVLWYSNRWVFGGTKLTVL
184.	VL-P of I2C	artificial	nt	GAGCTCGTTGTGACTCAGGAACCTTCACTCACTCACTCACTGGTGGACAGTCACACTCACTTG TGGCTCCTCGACTGGGCTGTACATCTGGCACTACCCAACTGGGTCCACAAAAACCCAGGTC AGGCACCCCGTGGTCTTAATAGTGGGACTAAGTCTCTGCCCCGGTACTCTGCCAGATTCTCA GGCTCCCTGCTTGAGGCAAGGCTGCCCTCACTCCTCAGGGGTACAGCCAGAGGATGAGGCAGA ATATTACTGTGTTCTATGGTACAGCAACCGCTGGGTGGTGGAGAACCAACTGACTGTCC TA

185.	VH-VL of I2C	artificial	aa	EVQLVESGGGLVQPFGSLKLSCAASGFTFNKYNMNVWRQAPGKLEWVARIRSKYNNYATYADS VKDRFTISRDDSKNTAYLQMNLLKTEDTAVYCVRHGNFGNSYISYWAYWGQGLTVTVSSGGGGS GGGSGGGGSGQTVVTPQPSLTVSPGGTVTLTCGSSSTGAVTSIGNYPNWWQKPGQAPRGLIGTKF LAPGTPARFSGSLGGKAALTLISGVQPEDEAEYVCVLWYSNRWVFGGKLTVL
186.	VH-VL of I2C	artificial	nt	GAGGTGCAGCTGGTCGAGTCTGGAGGAGGATGCTGCAGCCTGGAGGTCATTGAAACCTCATG TGCAGCCTCTGGATTACCTTCAATAAGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGTTGCTCCCATAGAAGTAATAATAATATGCAACATATTATGCCGATTCA GTGAAAGACAGGTTACCATCTCCAGAGATGATTCAAAAACACTGCCTATCTACAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTCTGTGTGAGACATGGAACTTCGGTAATAGCTACA TATCCTACTGGGCTTACTGGGGCCAGGGACTCTGGTCACCGTCTCCTCAGGTGGTGGTCTCT GGCGGCGGCTCCGGTGGTGGTCTCAGACTGTGTGACTCAGGAACCTTCACTCACCGT ATCACCTGGTGAACAGTCACTCTGTGGTCTCTGACTGGGCTGTACATCTGGCAACT ACCCAACTGGTCCAAACAAACCCAGGTACGGCAACCCGCTGTTAATAGTGGGACTAAGTTC CTGCCCCCGGTACTCTCTGCCAGATTCTCAGGCTCCCTGCTGGAGGCAAGGTCGCCCTCACCT CTCAGGGGTACAGCCAGAGGATGAGGCAGATAATTACTGTGTTCTATGTTACAGCAACCGCTGGG TGTTCCGTGGAGGAACCAACTGACTGTCTTA
187.	VH-VL-P of I2C	artificial	aa	EVQLLESGLVQPFGSLKLSCAASGFTFNKYNMNVWRQAPGKLEWVARIRSKYNNYATYADS VKDRFTISRDDSKNTAYLQMNLLKTEDTAVYCVRHGNFGNSYISYWAYWGQGLTVTVSSGGGGS GGGSGGGGSELVTPQPSLTVSPGGTVTLTCGSSSTGAVTSIGNYPNWWQKPGQAPRGLIGTKF LAPGTPARFSGSLGGKAALTLISGVQPEDEAEYVCVLWYSNRWVFGGKLTVL
188.	VH-VL-P of I2C	artificial	nt	GAGGTGCAGCTGCTCGAGTCTGGAGGAGGATGCTGCAGCCTGGAGGTCATTGAACTCTCATG TGCAGCCTCTGGATTACCTTCAATAAGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGTTGCTCGCATAGAAGTAATAATAATATGCAACATATTATGCCGATTCA GTGAAAGACAGGTTACCATCTCCAGAGATGATTCAAAAACACTGCCTATCTACAATGAACAA CTTGAAAACTGAGGACACTGCCGTGTACTCTGTGTGAGACATGGAACTTCGGTAATAGCTACA TATCCTACTGGGCTTACTGGGGCCAGGGACTCTGGTCACCGTCTCCTCAGGTGGTGGTCTCT GGCGGCGGCTCCGGTGGTGGTCTGAGCTGTTGTGACTCAGGAACCTTCACTCACCGT ATCACCTGGTGAACAGTCACTCATCTGTGGTCTCTGACTGGGCTGTACATCTGGCAACT ACCCAACTGGTCCAAACAAACCCAGGTACGGCAACCCGCTGTTAATAGTGGGACTAAGTTC CTGCCCCCGGTACTCTCTGCCAGATTCTCAGGCTCCCTGCTGGAGGCAAGGTCGCCCTCACCT CTCAGGGGTACAGCCAGAGGATGAGGCAGATAATTACTGTGTTCTATGTTACAGCAACCGCTGGG TGTTCCGTGGAGGAACCAACTGACTGTCTTA
189.	MCSP-G4 VH-VL x H2C VH-VL	artificial	aa	QVQLVQSGAEVKRPGASMKVSCKASGYTFNYYIHVWRQAPGQGLEWMGWINPNPNSGATNYAKFKQ GRVTMTRDTSTSTVYMESSLRSSEDTAVYYCAKSWVSWFASWGQGLTVTVSSGGGSGGGSGGG GSDIVMTQSPDSLAVSLGERATINCKSSQSVLSSNNRNLYAWYQKPGQPPKLLIYNASTRESG VPDRFSGSGSGTDFTLTISGLQAEDVAVYCCQHYSTFTFGPTKVDIKSGGGGSEVLVESGG GLVQPGGSLKLSCAASGFTFNKYNMNVWRQAPGKLEWVARIRSKYNNYATYADSVKDRFTISR

190.	MCSP-G4 VH-VL x H2C VH-VL	artificial	nt	<p>DDSKNTAYLQMNKLTEDTAVYYCVRHGNFGNSYISYWAYWQGTLVTSSGGSGSGGGGGGG SQTVVTQEPSTLTVSPGGTVTLTCGSSTGAVTSYYPNWVQKPGQAPRGLIGGTFKFLAPGTFARF SGSLLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGTKLTVL</p> <p>CAGGTGCAGCTGGTCCAGTCTGGGGCTGAGGTGAAGAGGCTCGGGCTCAATGAAGGTCTCCTG CAAGCTTCTGGGTACACCTTCAACCACTACTATATACACTGGTGCACAGGCCCTGGACAAG GTCTTGAGTGGATGGTGGATCAACCTTAACAGTGGTGGCCACAACTATGCACAGAAGTTCAG GGCAGAGTCACCATGACCAGGGACAGTCCACAGCACAGTCTACATGGAGCTGAGCAGCCTGAG ATCTGAGGACACGGCCGTGTTACTGTGCGAAATCCTGGGTCTCCTGGTTGCTTCTCGGGTCTC AAGAACCTTGGTCACCGTCTCCTCAGGTGGTGGTCTGCGGGCGGGCTCCGGTGGTGGT GGTCTGATATCGTGATGCCAGTCTCCAGACTCCTGGCTGTGTCTGTGGCGAGAGGCGCAC CATCAACTGCAAGTCCAGCCAGAGTGTCTTAAACAGCTCCAACAAATAGGAACACTTAGCTGGT ACCAGCAAAACAGGACAGCCTCCTAAGCTGCTCACTTACAGGATCTACCCGGGAATCCGGG GTCCCTGACCGATTGAGTGGCAGTCTGAGCGGGTCTGGGACAGATTTCACTCACCACAGTGGCTGCA GGCTGAAGATGTGGCAGTTTATTACTGTGCAACATATAGTACTCATTCACTTTGGCCCTG GGACCAAGTGATATCAAAATCCGAGGTGGTGGATCCGAGTGCAGCTGGTGGAGTCTGGAGGA GGATTGGTGACGCTGGAGGTCAATGAACTCTCATGTGCAGCTCTGGATTCACTTCAATAA GTACGCCATGAACCTGGTCCGCCAGGTCCAGGAAAGGTTTGAATGGTGTGCTCGCATAAAGAA GTAATATAATAATATGCAACATATATGCCGATTGAGTGAAGACAGGTTCAACATCTCCAGA GATGATTCAAAAACACTSCCTATCTACAAATGAACAACTTGAACACTGAGGACACTGCCGTGTA CTACTGTGTGAGACATGGAACTTCGGTATAGCTACATATCTACTGGCTTACTGGGGCCAAAG GGACTGTGGTCAACGCTCTCCTCAGGTGGTGGTCTGGCGGGCGGGCTCCGGTGGTGGTGGT TCTCAGACTGTTGTGACTCAGGAACCTTCACTCACCCTATCACCTGGTGAACAGTCACTCAC TTGTGGCTCCTCGACTGGGGCTGTTACATCTGGCTACTACCCAACTGGTCCACAAAAACAG GTCAGGCACCCGTGGTCTAATAGGTGGGACTAAGTCTCCTCGCCCGGTACTCCTGCCAGATTCT TCAGGCTCCCTGTGGAGGCAAGGTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGC AGAAATATTACTGTGCTCTATGGTACAGCAACCGCTGGGTGTTCCGGTGGAGGAACCAAACTGACTG TCCTA</p>
191.	MCSP-G4 VH-VL x F12Q VH-VL	artificial	aa	<p>QVQLVQSGAEVKRPGASMKVSCKASGYTFNTYITHWVRQAFQGLEWMGWINPNSGATNYAQKFQ GRVTMTRDTSTSTVYMEISSLRSEDYAVYYCAKSWVSWFASWQGTLTVSSGGSGSGGGSGGG GSDIVMTQSPDSLAVSLGERATINCKSSQSVLNSSNNRNYLAWYQKPGQPPKLLIYMASTRSG VPDRFSGSGSGTDFTLTISGLQAEADVAVYYCQHYSTPTFFPGTKVDIKSGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNSYAMNWVRQAPGKLEWVARIRSKYNNYATYYADSVKGRFTISR DDSKNTAYLQMNKLTEDTAVYYCVRHGNFGNSYISYWAYWQGTLVTSSGGSGSGGGSGGGG SQTVVTQEPSTLTVSPGGTVTLTCGSSTGAVTSYYPNWVQKPGQAPRGLIGGTFKFLAPGTFARF SGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGTKLTVL</p>
192.	MCSP-G4 VH-VL x F12Q VH-VL	artificial	nt	<p>CAGGTGCAGCTGGTCCAGTCTGGGGCTGAGGTGAAGAGGCTCGGGCTCAATGAAGGTCTCCTG CAAGCTTCTGGGTACACCTTCAACCACTACTATATACACTGGTGCACAGGCCCTGGACAAG</p>

<p>GTCTTGAGTGGATTGGATCAACCCCTAACAGTGGTCCACAAACTATGCACAGAAGTCCAG GGCAGACTCACCATGACCAGGGACACGTCCACGAGCACAGTCTACATGGAGCTGAGCAGCCTGAG ATCTGAGGACACGGCCGTGTATTACTGTGGAAATCCTGGGTCTCCTGGTTTGGTTTGGTCTCCTGGGTC AAGAACTTGGTCAACCGTCTCCTCAGGTGGTGGTCTGGCGCGCGGCTCGGTGGTGGT GGTCTGATATCGTGATGACCCAGTCTCCACACTCCCTGGCTGTGTCTCTGGCGGAGAGGCCAC CATCAACTGCAAGTCCAGCCAGAGTGTAAACAGCTCCAACTAGGAACACTACTAGCTGGT ACCAGCAAAACCAGGACAGCCTCCTAAGTGTCTTAACTGCTCATTTACTGGCATCTACCCGGGAATCCGGG GTCCCTGACCGATTGAGTGGCAGCGGTCTGGGACAGATTCACTCTCACCATCAGTGGCCTGCA GGCTAAAGATGTGGCAGTTTATTACTGTGAGCAACATTATAGTACTCATTCACTTTTGGCCCTG GGACAAAGTGGATACAAATCCGAGGTGGTGGATCCGAGGTGAGCTGGTGGTGGTGGAGGA GGATTGGTGCAGCCTGGAGGTCAATTGAACTCTCATGTGCAGCCTCTGGATTCACTTCACTCAATAG CTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGGTTTGGAAATGGGTGCTCGCATTAAGAA GTAATATATAATATGCAACATATTATGCCGATTGAGTGAAGGAGGTTTCCACTTCCACTTCCAGA GATGATTCAAAAACACTGCTCTATCTACAAATGAACAACTTGAACACTGAGGACACTGCCGTGTA CTACTGTGTGAGACATGGAACTTCGGTAAATAGTACTGTTCTGGCGCGCGGCTCCGGTGGTGGT GGACTGTGGTCACCGTCTCCTCAGGTGGTGGTCTGGCGCGCGGCTCCGGTGGTGGTGGT TCTCAGACTGTGTGACTCAGGAACCTTCACTACCGTATCACCTGGTGAACAGTCACTCACTCAC TTGTGGTCTCTGACTGGGCTGTACATCTGCAACTACCAACTGGGTCCAAACAAACACAG CTCAGCCACCCCTGGTCTAATAGTGGACTAAGTCTCTGCCCGGCTACTCTCCACACTTC TCAGGCTCCCTGCTTGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGC AGAATATTACTGTGTTCTATGTTACAGCAACCGCTGGTGGTTCGGTGGAGAACCAACTGACTG TCTTA</p>		<p>QVQLVQSGAEVKRPGASMKVSKASGYTFTNYYIHVVRQAPGQGLEWMGWINPNSGATNYAQKFQ GRVTMTRDTSTSTVYME LSSLRSEDTAVYCAKSWSFASWGQGLTVTVSSGGSGSGSGSGG GSDIVMTQSPDSLAVSLGERATINCKSSQSVLNSSNNRNYLAWYQQKPGQPPKLLIYNASTRESG VPDRFSGSGGTDFLTISGLQAEDEVYVYQQHYSTPFTFGPGTKVDIKSGGGSEVQLVESGG GLVQPGGSLKLSAASGFTFNKYAMNVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNNIKTEDTAVYVCVRHGFNYSYI SYWAYWGQGLTVTVSSGGSGSGSGSGSGG SQTIVTQEPSTLTVSPGGTITLTGSSSTGAVTSGNYPNWVQKPGQAPRGLIGGTGKFLAPGTPARF SGSLGKGKAALTLSGVQPEDEAEYCYVLMYSNRWVFGGTKLTVL</p>
<p>193.</p>	<p>MCSP-G4 VH-VL x I2C VH-VL</p>	<p>aa</p>
		<p>nt</p>
<p>194.</p>	<p>MCSP-G4 VH-VL x I2C VH-VL</p>	<p>artificial</p>

55	195.	MCSP-G4 VH-VL-P x F6A VH-VL-P	artificial	aa	<p>CATCAACTGCAAGTCCAGCCAGAGTGTCTTAAACAGCTCCAACAATAGGAACACTACTTAGCTGGT ACCAGCAAAAACAGGACAGCCTCCTAAGCTGCTCATTTACTGGCATCTACCCGGGAATCCGGG GTCCCTGACCGATTTCAGTGGCAGCGGTCTGGACAGATTTCACCTCACCATAGTGGCCTGCA GGCTGAAGATGTGGCAGTTTATTTACTGTCAACAATATAGTACTCCATTCACTTTTGGCCTG GGACCAAGTGATATCAAAATCCGGAGGTGGTGGATCCGAGGTGAGCTGGTCGAGTCTGGAGGA GGATTGGTGAGCCTGGAGGTTCATTGAACCTCTCATGTGCAGCCTCTGGATTACCTTCAATAA GTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAGGTTTGAATGGTGTCTCGCATAAAGAA GTAATAATAATAATTATGCAACATATTATGCCGATTTCAGTGAAGACAGGTTACCATCTCCAGA GATGATTCAAAAACACTGCCTATCTACAAATGAACAACCTTGAAACTGAGGACACTGCCGTGTA CTACTGTGTGAGACATGGAACTTCGGTATATAGTACATATCCTACTGGCTTACTGGGCAAG GGAATCTGTGACCGTCTCCTCAGGTGGTGGTGTCTGGCGGCGGCTCCGGTGGTGGT TCTCAGACTGTGTGACTCAGGAACCTTCACTACCGTATCACCTGGTGAACAGTCACTCAC TTGTGGCTCCTCGACTGGGCTGTACATCTGGCAACTACCAAACTGGTCCACAAAAAACAG GTCAGGCACCCCGTGGTCTAATAGGTGGGTAAGTCTCCTGCCCGGTACTCCTGCCAGATT TCAGGCTCCCTGCTTGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGC AGAAATATTACTGTGTTCTATGTTACAGCAACCGTGGTGTTCGGTGGAGGAACCAAACTGACTG TCCTA</p>
40					<p>QVQLVQSGAEVKRPGASMKVSKASGYTFTNYYTHWVRQAPQGLEWGMWINPNSGATNYAQKFQ GRVTMRDSTSTVYMESSLRSEDVAVYCAKSWVSWFASWGQTLTVTVSSGGSGGGSGGG GSELVMTQSPDLSAVSLGERATINCKSSQSVLNSSNNRNYLAWYQQKPGQPKLLIYNASTRESG VPDRFSGSGSTDFTLTISGLQAEDEVAVYCOQHSTPFTFGPTKVDIKSGGGSEVQLLES GLVQPGGSLKLSCAASGFTFNIYAMNVRQAPEGLEWVARIRSKYNNYATYYADSVKSRFTISR DDSKNTAYLQMNLLKTEDTAVYYCVRHGNFNSYVFFAYWGQTLTVTVSSGGSGGGSGGG SELVYEQEPLSTVSPGGTTLTTCGSSTGAVTSGYYPNWVQKPGQAPRGLIGGTKFLAPGTPARF SGSLLGKKAALTLSGVQPEDEAEYYCALWYSNRWVFGGTLLTVL</p>
45	196.	MCSP-G4 VH-VL-P x F6A VH-VL-P	artificial	nt	<p>CAGGTGAGCTGGTCCAGTCTGGGCTGAGGTGAAGAGCCCTGGGCTCAATGAAGTCTCCTG CAAGGCTCTGGGTACACCTTCAACCACTACTATATACACTGGTGGCGACAGGCCCTTGACAAG GTCTTGAGTGGATGGTGGATCAACCCCTAACAGTGGTGGCCACAACTATGCACAGAGTCCAG GGCAGAGTCACCATGACCAGGGACACGTCCACGAGCAGACACTACATGGAGCTGAGCAGCTGAG ATCTGAGGACACGGCCGTGTATTACTGTGGAATCTGGTCTCCTGGTTGCTTCTCCTGGGTC AAGGAACCTTGGTCAACCGTCTCCTCAGGTGGTGGTGTCTGGCGGCGGCTCCGGTGGTGGT GGTCTGAGCTCGTGTGATGACCCAGTCTCCAGACTCCCTGGCTGTGTCTCTGGCGAGAGGCGAC CATCAACTGCAAGTCCAGCCAGAGTGTCTTAAACAGCTCCAACAATAGGAACACTTAGTGGT ACCAGCAAAAACAGGACAGCCTCCTAAGTGTGCTATTACTGGCATCTACCCGGGAATCCGGG GTCCCTGACCGATTTCAGTGGCAGCGGTCTGGACAGATTTCACCTCACCATCAGTGGCCTGCA GGCTGAAGATGTGGCAGTTTATTACTGTCAAGCAACATATAGTACTCCTTCACTTTTGGCCTG GGACCAAGTGATATCAAAATCCGGAGGTGGTGGATCCGAGGTGAGCTGCTCGAGTCTGAGGA</p>

55					<p>GGATTGGTGAGCCTGGAGGGTCATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAATAT CTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGGTTTGAATGGGTGCTCGCATAAAGAA GTAAATATAAATAATATGCAACATAATTATCGCAATTCAGTGAAAGCAGGTTTCAACATCTCCAGA GATGATTCAAAAACACTGCCTATCTACAAATGAAACAACTTGAAACTGAGGACACTGCCCTGTA CTACTGTGTGAGACATGGGAACCTTCGGTAATAGCTACGTATCCTTCTTCTGCTTACTGGGCAAG GGACTCTGGTCACCGTCTCCTCAGGTGGTGGTCTGGCGGGGGCTCCGGTGGTGGTGGT TCTGAGCTCGTGTGACTCAGGAACCTTCACTACCGTATCACCTGGTGAACAGTCACTCAC TTGTGGCTCCTCGACTGGGCTGTTACATCTGCTACTACCAAACTGGGTCCAAACAAAACCCAG GTCAGGCACCCGCTGTTAATAGGTGGGACTAGCTCCTCGCCCCGCTACTCCTGCCAGATTCTC TCAGGCTCCCTGCTTGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGC AGAAATATTACTGTGCTCTATGGTACAGCAACCGCTGGGTGTTTCGGTGGAGGAACCAAACTGACTG TCCTA</p>
50	MCSP-G4 VH-VL-P x H2C VH-VL-P	artificial	aa		<p>QVQLVQSGAEVKRPGASMKVSKASGYFTNYIYIHWRQAPGQGLEWMGNINPNSGATNYAQKFQ GRVTMTRDTSSTVYMELSSLRSEDTAVYCAKSWSFASWGQTLTVTVSSGGSGGGSGGG GSELVMTQSPDSLAVSLGERATINCKSSQSVINSSNNPNYLAWYQQKPPKLLIYWASTRESG VPDRFSGSGSTDFTLTISGLQAEDVAVYCCQHYSTPTFTGPGTKVDIKSGGGGSEVQLLES GLVQPGGSLKLSCAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNMLKTEDTAVYICVRHGFNSYISYWAYWGQTLTVTVSSGGSGGGSGGGGG SELVVTQEPSTLTVSPGGTVTLTCSGSTGAVTSGYYPNWVQQKPGQAPRGLIGGTKFLAPGT PARFSGSLLGKKAALTLSGVQPEDEAEYICALWISNRWVFGGKLTIVL</p>
45	MCSP-G4 VH-VL-P x H2C VH-VL-P	artificial	nt		<p>CAGGTGCAGCTGGTCCAGTCTGGGGCTGAGGTGAAGAGCCTGGGGCTCAATGAAGGTCTCTCTG CAAGGCTTCTGGGTACACCTTCACCAACTACTATATACACTGGTGCACAGGCCCTTGACACAAG GTCTTGAGTGGATGGGTGGATCAACCTAACAGTGGTCCCAAACTATGCACAGAACTCCAG GGCAGAGTCACCATGACCAGGACACGTCCACGAGCACAGTCTACATGGAGCTGAGCAGCCTGAG ATCTGAGGACACGGCCGTGTATTACTGTGCGAAATCCTGGGTCTCCTGGTTTGTCTTCTGGGTC AAGGAACCTTGGTCACCGTCTCCTCAGGTGGTGGTCTGGCGGGCGGCTCCGGTGGTGGT GGTCTGAGCTCGTGATGACCCAGTCTCCAGACTCCTGGCTGTGTCTCTGGCGGAGAGGCCAC CATCAACTGCAAGTCCAGCCAGAGTGTTTAAACAGCTCCAACAATAGGAACACTACTTGGT ACCAGCAGAAACCCAGGACAGCCTCCTAAGTCTGCTTACTGGGATCTACCCGGGAATCCGGG GTCCCTGACCGATTTCAGTGGCAGCGGTCTGGGACAGATTTCACTCTCAACATCAGTGGCTGCA GGTGAAGATGTGGCAGTTTATTACTGTGCAACAATATAGTACTCCATTCACTTTTGGCCCTG GGACCAAGTGGATATCAAAICCGGAGGTGGTGGATCCGAGGTGCAGTGTCTCGAGTCTGGAGGA GGATTGGTGCAGCCTGGAGGTCATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAATAA GTACGCCATGAACCTGGTCCGCCAGGCTCCAGAAAGGTTTGAATGGGTGCTCGCATAAAGAA GTAAATATAAATAATATGCAACATAATTATGCCGATTCAGTGAAGACAGGTTTCAACATCTCCAGA GATGATTCAAAAACACTGCCTATCTACAAATGAACAACTTGAAACTGAGGACACTGCCGTGTA CTACTGTGTGAGACATGGGAACCTTCGGTAATAGTACATATCTACTGGGCTTACTGGGGCCAAAG</p>

199.	MCSP-G4 VH-VL-P x H1E VH-VL-P	artificial	aa	<p> GGACTCTGGTCACCGTCTCCTCAGGTGGTGGTGGTCTTGGCGGGGGGGCTCCGGTGGTGGTGGT TCTGAGCTCGTTGTGACTCAGGAACCTTCACTCACCGTATCACCTGGTGGAACACTCACACTCAC TTGTGGCTCTCGACTGGGCTGTTACATCTGGTACTACCCAACTGGTCCAAACAAAAACACAG GTCAGGCACCCCGTGGTCTAATAGGTGGGACTAAGTCTCGCCCCGGTACTCTCGCCAGATTCT TCAGGCTCCCTGCTTGGAGCAAGGTCGCCCTCACCTCTCAGGGGTACAGCCAGAGATGAGGC AGAATATTACTGTCTCTATGGTACAGCAACCGTGGTGGTCTCGGTGGAGGACCAAACTGACTG TCCTA </p> <p> QVQLVSGAEVKRPGASMKVSCKASGYTFTNYYIHWRVQAPGQGLEWMGWINFNSGATNYAQKFQ GRVTMTRDSTSTVYMEISSLRSEDVAVYYCAKSWSWFASWQDGLTVTVSSGGSGSGSGSGG GSELVMTQSPDLSAVSLGERATINCKSPQSVLNSNNRNLYAWYQKPGQPPKLLIYWASTRESG VPDRFSGSGSGTDFTLTISGLQAEDEVAVYYCQOHYSTFTFTGPGTKVDIKSGGGGSEVQLLES GLEQPGGSLKLSAASGFTFNSYAMNWRVQAPKGLIEWVARIRSKYNNYATYYADSVKGRFTISR DDSKNTAYLQMNNILKTEDTAVYYCVRHGFNGFNSYLSFWAYWGQGLTVTVSSGGSGSGSGSGG SELVVTQEPSLTVSPGGTVTLTCSGSTGAVTSGYFNVWVQKPGQAPRGLIIGGTRFLAPGTPARF SGSLGGKZAAITLSGVQPEDEAEYYCALWYSNRWVFGGGTKLTVL </p>
200.	MCSP-G4 VH-VL-P x H1E VH-VL-P	artificial	nt	<p> CAGGTGCAGCTGGTCCAGTCTGGGGCTGAGGTGAAGAGCGCTGGGGCTCAATCAAGGTCCTCCTG CAAGGCTTCTGGGTACACCTTCACCAACTACTATATACACTGGGTGGACAGGCCCTGGACAAG GTCTTGAGTGGATGGGTGGATCAACCCCTAACAGTGGTGCCACAACTATGCACAGAGTTCACAG GGCAGAGTCAACATGACCAGGGACACGTCCACAGACAGCTCTACATGGAGTGCAGAGCCTGAG ATCTGAGGACACGGCCGCTGTTACTGTGCGAATCCTGGGTCTCCTGGTGGTCTCCTGGGTGGT AAGGAACCTTGGTCAACGCTCCTCAGGTGGTGGTGGTGGTGGCGGGGGGCTCCGGTGGTGGT GGTCTGAGCTCGTGATGACCCAGTCTCCAGACTCCCTGGCTGTGTCTCTGCGGCGAGAGGCCAC CATCAACTGCAAGTCCAGCCAGAGTGTCTTAAACAGCTCCAACAATAGGAACACTACTAGCTTGGT ACCAGCAGAACACAGGACAGCCTCCTAAGCTGCTCATTTACTGGCATCTACCCGGGAATCCGGG GTCCCTGACCGATTTCAGTGGCAGCGGTCTGGGACAGATTTCACTCTCACCATCAGTGGCCTGCA GGCTGAAGATGTGGCAGTTTATTACTGTACGAAACATTATAGTACTCAATTCATTTGGCCCTG GGACAAAGTGGATATCAAAATCCGGAGGTGGTGGATCCGAGGTGCAGTGTCTGAGTCTGGAGGA GGATTGGAGCAGCCTGGAGGTCAATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAATTC GTACGCCATGAATGGGTCCGCCAGGTCCAGGAAAGGTTTGGAAATGGTGTGCTCGCATAAAGAA GTAATATAATAATTATGCAACATATTATGCCGATTTCAGTGAAGGGAGGTTTCACATCTCCAGA GATGATTCAAAAAACACTGCCTATCTACAAATGAACAACTTGAAACACTGAGGACACTGCCGTGTA CTACTGTGTGAGACATGGGAACTTCGGTAATAGTACTCTTCCTTGGCTTACTGGGCCCAAG GGACTGTGTACCGTCTCCTCAGTGGTGGTGGTGTCTGGCGGGCGGGCTCCGGTGGTGGTGGT TCTGAGCTCGTTGTGACTCAGGAACCTTCACTACCGTATCACCTGGTGAACAGTGCACACTCAC TTGTGGCTCCTCGACTGGGCTGTTACATCTGGTACTACCCAACTGGGTCCCAACAAAAACACAG GTCAGGCACCCCGTGGTCTAATAGGTGGGACTAAGTTCCTCGCCCCGGTACTCCTGCGAGATTCT TCAGGCTCCCTGCTTGGAGGCAAGGTGCCCTCACCTCTCAGGGGTACAGCCAGCATGAGGC </p>

201.	MCSP-G4 VH-VL-P x G4H VH-VL-P	artificial	aa	<p>AGAATATTACTGTCTCTATGTTACAGCAACCGCTGGGTGTTCCGGTGGAGGAACCAAACTGACTG TCCTA</p> <p>QVQLVQSGAEVKRPGASMKVSCKASGYFTFTNYIHWVRQAPQGQLEWMGWINPNSGATNVAQKFQ GRVTMRDTSSTVYMEISSLRSEDYAVYCAKSWVSWFASWGQGLTVTVSSGGSGSGSGSGG GSELVMTQSPDSLAVSLGERATINCKSSQSVLNSSNNRNLYAWYQQKPGQPPLKLLIYNASTRESG VPDRFSGSGSTDEFTLTISGLQAEADVYCCQHYSTPTFPQGTVDIKSGGGSEVQLLES GLVQPGGSLKLSAASGFTFNRYAMNWVRQAPKGLWVARIRSKYNNYATYYADSVKGRFTISR DDSKNTAYLQMNIKTEDTAVYCVRHGNEFNSYLSYFAYWGQGLTVTVSSGGSGSGSGSGGGG SELVITQEPSTLVSPGGTVTLTCSSTGAVTSGYYPNWVQKPGQAPRGLIGGTRKFLAPGTPARF SGSLGGKAALTLSGVQPEDEAEYICALWYSNRWVFGGTKLTVL</p> <p>CAGGTGACGCTGGTCCAGTCTGGGGCTGAGGTGAAGAGGCTGGGGCTCAATGAAGGTCTCCTG CAAGGCTTCTGGGTACACCTTACCAACTACTATATACACTGGTGCACAGGCCCTGGACAAG GTCTTGAGTGATGGGTGGATCAACCTTAACAGTGGTCCACAACTATGCACAGAGTTCAC GGCAGAGTCACCATGACACGAGGACAGTCCACGACAGCATCTACATGGAGCTGAGACGCTGAG ATCTGAGGACACGGCCGTGTATTACTGTGCGAAATCCTGGGTCTCCTGGTTGCTTCTGGGGT AAGGAACCTTGGTCAACGCTCTCCTCAGGTGGTGGTCTTGGCGGGGGGCTCCGGTGGTGGT GGTCTGAGCTCGTGATGACCCAGTCTCCAGACTCCCTGGTGTGTCTCTGGCGGAGAGGCCAC CATCAACTGCAAGTCCAGCCAGAGTGTAAACAGCTCCAACAATAGGAATCTAGCTTGGT ACCAGAGAAACACGACAGCTCTAAGCTGCTATCTAGTGGCATCTACCGGGAATCCGGG GTCCCTGACCGATTAGTGGCAGGGGTCTGGACAGATTTCACTCTCACTACATGAGTGGCTGCA GGCTGAAGATGTGGCAGTTTATTACTGTGACCAACATTAAGTACTCATTCACTTTGGCCCTG GGACCAAGTGATATCAATCCGGAGGTGGTGGATCCGAGGTGCAGCTGCTCGAGTCTGGAGGA GGATTGGTCAGCTGGAGGTCAATGAACTCTCATGTGCAGCTCTGGATTCACCTCAATCG CTACGCCATGAACCTGGTCCGCCAGGCTCCAGAAAGGGTTTGAATGGGTGCTCGCATAAAGAA GTAATATAATAATATGCAACATATTATGCCGATTGAGTGAAGGAGGTTTACCATCTCCAGA GATGATCAAAAACACTGCCTATCTACAAATGAACAACCTGAAAACCTGAGGACACTGCCGTGTA CTACTGTGTGAGACATGGGAACCTCGGTAAATAGTACTATCTTACTTCCGTTACTGGGGCCAAAG GGACTCTGGTCACCGTCTCCTCAGGTGGTGGTCTTGGCGGGGGGGCTCCGGTGGTGGTGGT TCTGAGCTCGTTGTGACTCAGGAACCTTCACTACCGGTATCACCTGGTGAACAGTCACTCAC TTGTGGCTCCTCGACTGGGCTGTACATCTGGTACTACCAAACTGGTCCAAACAAAACCCAG GTCAGGACACCCGTGGTCTAATAGGTGGGACTAAGTTCTCGCCCCGGTACTCTGCCAGATTC TCAGGCTCCCTGCTTGGAGCAAGGTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGC AGAAATATTACTGTCTCTATGTTACAGCAACCGCTGGGTGTTCCGGTGGAGGAACCAAACTGACTG TCCTA</p>
202.	MCSP-G4 VH-VL-P x G4H VH-VL-P	artificial	nt	
203.	MCSP-G4 VH-VL-P x A2J VH-VL-P	artificial	aa	<p>QVQLVQSGAEVKRPGASMKVSCKASGYFTFTNYIHWVRQAPQGQLEWMGWINPNSGATNVAQKFQ GRVTMRDTSSTVYMEISSLRSEDYAVYCAKSWVSWFASWGQGLTVTVSSGGSGSGSGSGG GSELVMTQSPDSLAVSLGERATINCKSSQSVLNSSNNRNLYAWYQQKPGQPPLKLLIYNASTRESG</p>

204.	MCSP-G4 VH-VL-P x A2J VH-VL-P	artificial	nt	<p>VPDRFSGSGSGTDFTLTISGLQAEADVAVYCCQHYSTPFTFGPGTKVDIKSGGGGSEVQLLES</p> <p>GLVQPGGSLKLSCAASGFTFNVMWVRQAPGKLEWVARIRSKYNNYATYYADSVKRFETISR</p> <p>DDSKNTAYLQMNLLKTEDTAVYCVVRHGFNGSYLSWYWGQGLTVTVSSGGSGSGSGGGG</p> <p>SELVVTQEPSTVSPGGTTLTCSRSTGAVTSGYYPNWWQKPGQAPRGLIGATDMRPSGTPARF</p> <p>SGSLLGGKAAITLSGVQPEDEAEYYCALWYSNRWVFGGTKLTVL</p> <p>CAGGTGCAGCTGGTCCAGTCTGGGGTGGGTGAAGAGGCCTGGGGCTCAATGAAGTCTCCTG</p> <p>CAAGGCTTCTGGGTACACCTTCACCAACTACTATATACACTGGTGGACAGGCCCTGGACAAG</p> <p>GTCTTGAGTGGTGGTGGATCAACCTAACAGTGGTGGCCACAACACTATGCACAGAAGTTCAG</p> <p>GGCAGAGTCACCATGACAGGACACGTCACGACGACAGTCTACATGGAGCTGAGAGCCTGAG</p> <p>ATCTGAGGACACGGCGTGTATTACTGTGCGAAATCCTGGGTCTCCTGTTGCTCCTGGGTC</p> <p>AAGGAACCTTGTCAACGCTCCTCAGGTGGTGGTGTCTGGCGGGGGCTCCGGTGGTGGT</p> <p>GGTCTGAGCTCGTATGACCCAGTCTCCAGACTCCTGGTGGTGTCTCTGGGCGAGAGGGCCAC</p> <p>CATCAACTGCAAGTCCAGCCAGAGTGTTTAAACAGCTCCAACAATAGGAACACTAGCTTGGT</p> <p>ACCAGCAAAACAGGACAGCCTCCTAAGCTGCTATTACTGGCATCTACCCGGGAATCCGGG</p> <p>GTCCCTGACCGATTGAGTGGCAGCGGTCTGGGACAGATTCACTCTCACCATCATGTCCTGCA</p> <p>GGCTGAAGATGGCAGTTTATTACTGTGCAACAATATAGTACTCATTCACTTTGGCCCTG</p> <p>GGACCAAGTGAATCAAAATCCGGAGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGT</p> <p>GGATTGGTGCAGCTGGAGGGTCAATGAAACTCAATGTCAGCTTGGATTCACTTCAATGT</p> <p>CTACGCCATGAAGTGGTCCGCCAGGCTCCAGGAAAGGTTTGGATTGGTGGTGGTGGTGGT</p> <p>GTAATATAATAATATGCAACATATTATGCCGATTGAGTGAAGAGGTTTCAACATCTCCAGA</p> <p>GATGATTCAAAAACACTGCCTATCTACAAATGAACAATGAAACTGAGGACACTGCGGTGTA</p> <p>CTACTGTGTGACATGGAACTTCGGTAAATAGTACTTATCTGGTGGCTTACTGGGGCCCAAG</p> <p>GGACTCTGGTCAACGCTCCTCAGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGT</p> <p>TCTGAGCTCGTGTGACTCAGGAACCTTCACTACCGTATACCTGGTGGAACTCACTCAC</p> <p>TTGTGGCTCCTCGACTGGGCTGTACATCTGGCTACTACCAAACTGGGTCCAAACAAACCCAG</p> <p>GTCAGGCACCCCGTGGTCTAATAGTGGCTGACATGAGGCCCTCTGGTACTCCTGCCAGATT</p> <p>TCAGGCTCCCTGCTGGAGGCAAGCTGCCCTCACCCTCAGGGGTACAGCCAGAGGATGAGGC</p> <p>AGAAATATTACTGTGCTCTATGTTACAGCAACCGCTGGGTGGTGGTGGTGGTGGTGGTGGT</p> <p>TCCTA</p>
205.	MCSP-G4 VH-VL-P x E1L VH-VL-P	artificial	aa	<p>QVQLVQSGAEVKRPGASMKVSCASGYFTFTNYIHWVRQAPGQGLEWMGWINPNSGATNYAQKFQ</p> <p>GRVTMTRDTSTSTVYMEISSLRSEDTAVYCAKSWVSWFASWGQGLTVTVSSGGSGSGSGGGG</p> <p>GSELVMTQSPDSLAVSLGERATINCKSSQSVLNNRNLYAWYQKPGQPKLLIYWASTRESG</p> <p>VPDRFSGSGSGTDFTLTISGLQAEADVAVYCCQHYSTPFTFGPGTKVDIKSGGGGSEVQLLES</p> <p>GLVQPGGSLKLSCAASGFTFNVMWVRQAPGKLEWVARIRSKYNNYATYYADSVKRFETISR</p> <p>DDSKNTAYLQMNLLKTEDTAVYCVVRHGFNGSYLSWYWGQGLTVTVSSGGSGSGSGGGG</p> <p>SELVVTQEPSTVSPGGTTLTCSRSTGAVTSGYYPNWWQKPGQAPRGLIGATDMRPSGTPARF</p> <p>SGSLLGGKAAITLSGVQPEDEAEYYCALWYSNRWVFGGTKLTVL</p>

206.	MCSP-G4 VH-VL-P x E1L VH-VL-P	artificial	nt	<p>CAGTGCAGCTGGTCCAGTCTGGGGCTGAGGTGAAGAGGCCCTGGGGCTCAATGAAGGTCTCTG CAAGGCTTCTGGGTACACCTTCAACCACTACTATATACACTGGTGGCGACAGGCCCTGGACAAG GTCTGAGTGGATGGTTGGATCAACCTAACAGTGGTGGCCACAAATATGACAGCAAGTCCAG GGCAGAGTCAACCATGACCAGGACACGTCCACAGACACAGTCTACATGGAGCTGAGCAGCCTCAG ATCTGAGGACACGGCCGTGTATTACTGTGCGAATCTCTGGTCTCCTGGTTTGTCTTCTGGGCTC AAGGAACCTTGGTCAACCTCTCTCAGTGGTGGTGGTCTGGCGGGGGCTCCGGTGGTGGT GGTCTGAGCTCGTATGACCCAGTCTCCAGACTCCCTGGCTGTCTCTGGGCGAGAGGGCCAC CATCAACTGCAAGTCCAGCCAGAGTGTAAACAGCTCCACAAATAGGAACACTACTAGTCTGGT ACCAGCAAAACAGGACAGCCTCTAAGTGTCTATTTACTGGCATCTACCCGGGAATCCGGG GTCCCTGACCGATTGAGTGGCAGCGGTCTGGGACAGATTCACTCTCACCATCAGTGGCTGCA GGTGAAGATGTGGCAGTTTATTACTGTGCAACATATAGTACTCCTTCACTTCTGGCCCTG GGACCAAGTGGATATCAATCCGAGGTGGTGGATCCGAGGTGAGTCTGCTCGAGTCTGGAGGA GGATTGGTGCAGCCTGGAGGTCTTGAACCTCTCATGTGAGCCTCTGGATTCACTTCAATTA GTACGCCATGAACCTGGTCCGCCAGGTCCAGAAAGGTGGAAATGGGTGCTCGCATTAAGAA GTAAATATAATAATTATGCAACATATTATGCCGATTGAGTGAATCGAGGTTCACCATCTCCAGA GATGATTCAAAAACACTGCTCTATCTACAAATGAACAACTTGAACACTGAGGACACTGCCGTGTA CTACTGTGAGACATGGAACTTCGTAATAGCTACACATCTTACTACGCTTACTGGGCGCAAG GGAATCTGGTCAACCGTCTCTCAGTGGTGGTGGTCTGGCGGGGGCTCCGGTGGTGGTGGT TCTGAGCTCGTTGTCACTACCAACCTTCACTACCTCATCCTGCTGCAACAGTCACTCAC TTGTGGTCTCTCGACTGGGTGTTACATCTGGCTACTACCAAACTGGGTCCAAACAAACAG GTCAGGACACCCGTGGTCTAATAGTGGGACTAAGTCTCTGCCCCGGTACTCTCTGCCAGATT TCAGGCTCCCTGCTTGAGGCAAGGTGCCCTCAGCTCTCAGGGTACAGCCAGAGGATGAGGC AGAATATTACTGTGCTCTATGGTACAGCAACCGTGGTGTTCGGTGGAGGAACCAAACTGACTG TCTTA</p>
207.	MCSP-G4 VH-VL-P x E2M VH-VL-P	artificial	aa	<p>QVQLVQSGAEVKRPGASMKVSCKASGYTFNTYYIHWRQAPGQGLEWMGWNPNSGATNYAQKFQ GRVTMTRDTSTSTVYMEISSLRSEDTAVYCAKSWVSWFASWGOGTLTVSSGGGGGGGGGGGG GSELVMTQSPDLSAVSLGERATINCKSSQSVLNSSNNRNLYAWYQQKPGQPPLLIYMASTRESG VPDRFSGSGGTDFTLTISGLQAEDVAVYCCQHYSTPTFTFGPTKVDIKSGGGGSEVQLLES GLVQPGGSLKLSCAASGFTFNGYAMNWRQAPGKLEWVARIRSKYNNYATYYADSVKERTISR DDSKNTAYLQMNLIKTEAVYCVHRNFGNSYLSWFAWYQGQTLTVSSGGGGGGGGGGGGGG SELVVTQEPSTLTVSPGGTTLTCSRSTGAVTSGYYPNWVQKPGQAPRGLIGATDMRPSGTPARF SGSLLGKKAALTLSGVQPEDEAEYICALWYSNFWVFGGTGKLTVL</p>
208.	MCSP-G4 VH-VL-P x E2M VH-VL-P	artificial	nt	<p>CAGTGCAGCTGGTCCAGTCTGGGGCTGAGGTGAAGAGGCCCTGGGGCTCAATGAAGGTCTCTG CAAGGCTTCTGGGTACACCTTCAACCACTACTATATACACTGGTGGCGACAGGCCCTGGACAAG GTCTGAGTGGATGGTTGGATCAACCTAACAGTGGTGGCCACAAATATGACAGCAAGTCCAG GGCAGAGTCAACCATGACCAGGACACGTCCACAGACACAGTCTACATGGAGCTGAGCAGCCTCAG ATCTGAGGACACGGCCGTGTATTACTGTGCGAATCTCTGGTCTCCTGGTTTGTCTTCTGGGCTC AAGGAACCTTGGTCAACCTCTCTCAGTGGTGGTGGTCTGGCGGGGGCTCCGGTGGTGGT GGTCTGAGCTCGTATGACCCAGTCTCCAGACTCCCTGGCTGTCTCTGGGCGAGAGGGCCAC CATCAACTGCAAGTCCAGCCAGAGTGTAAACAGCTCCACAAATAGGAACACTACTAGTCTGGT ACCAGCAAAACAGGACAGCCTCTAAGTGTCTATTTACTGGCATCTACCCGGGAATCCGGG GTCCCTGACCGATTGAGTGGCAGCGGTCTGGGACAGATTCACTCTCACCATCAGTGGCTGCA GGTGAAGATGTGGCAGTTTATTACTGTGCAACATATAGTACTCCTTCACTTCTGGCCCTG GGACCAAGTGGATATCAATCCGAGGTGGTGGATCCGAGGTGAGTCTGCTCGAGTCTGGAGGA GGATTGGTGCAGCCTGGAGGTCTTGAACCTCTCATGTGAGCCTCTGGATTCACTTCAATTA GTACGCCATGAACCTGGTCCGCCAGGTCCAGAAAGGTGGAAATGGGTGCTCGCATTAAGAA GTAAATATAATAATTATGCAACATATTATGCCGATTGAGTGAATCGAGGTTCACCATCTCCAGA GATGATTCAAAAACACTGCTCTATCTACAAATGAACAACTTGAACACTGAGGACACTGCCGTGTA CTACTGTGAGACATGGAACTTCGTAATAGCTACACATCTTACTACGCTTACTGGGCGCAAG GGAATCTGGTCAACCGTCTCTCAGTGGTGGTGGTCTGGCGGGGGCTCCGGTGGTGGTGGT TCTGAGCTCGTTGTCACTACCAACCTTCACTACCTCATCCTGCTGCAACAGTCACTCAC TTGTGGTCTCTCGACTGGGTGTTACATCTGGCTACTACCAAACTGGGTCCAAACAAACAG GTCAGGACACCCGTGGTCTAATAGTGGGACTAAGTCTCTGCCCCGGTACTCTCTGCCAGATT TCAGGCTCCCTGCTTGAGGCAAGGTGCCCTCAGCTCTCAGGGTACAGCCAGAGGATGAGGC AGAATATTACTGTGCTCTATGGTACAGCAACCGTGGTGTTCGGTGGAGGAACCAAACTGACTG TCTTA</p>

[illegible]

				<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p>
<p>GGCTGAGATGTGGCAGTTTATTACTGTGTCAGCAACATTATAGTACTCCATTCACTTTTGGCCCTG</p> <p>GGACCAAAGTGGATATCAAAATCCGGAGGTGGTGGATCCGAGGTGCAGTCTCGAGTCTGGAGGA</p> <p>GGATTGGTGCAGCTGGAGGTCAATGAACTCTCATGTGCAGCCTCTGGATTCACTTCAATGT</p> <p>GTACGCCATGAACCTGGTCCGCCAGGTCCAGGAAAGGTTTGAATGGTGTGTCGCATAAGAA</p> <p>GTAATATAATAATATGCAACATATTATGCCGATTCAGTGAAAAAGAGTTTCAACATCTCCAGA</p> <p>GATGATCAAAAAACACTGCCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTA</p> <p>CTACTGTGTGAGACATGGAACTTCGGTAATAGTACATATCTGTGGCTTACTGGGCCAAG</p> <p>GGACTGTGTCACCGTCTCCTCAGGTGGTGGTCTGGCGGGGGCTCCGGTGGTGGTGGT</p> <p>TCTGAGCTGTTGTGACTCAGGAACCTTCACTCACCCTATCACCTGGTGAACAGTCACTCAC</p> <p>TTGTGGCTCCTCGACTGGGCTGTTACATCTGCTACTACCCAACTGGTCCCAACAAAACCCAG</p> <p>GTACGACACCCCGTGTCTAATAGGTGGGACTAAGTCTCTGCCCGGTACTCTCTGCCAGATTCT</p> <p>TACGGTCCCTGCTTGGAGCAAGGTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGC</p> <p>AGAAATATTACTGTGCTCTATGGTACAGCAACCCCTGGGTGTTCTGGTGGAGGAACCAACTGACTG</p> <p>TCCTA</p>	aa	artificial	<p>MCSP-G4 VH-VL-P</p> <p>x F12Q VH-VL</p>	<p>211.</p>
<p>QVQLVQSGAEVKRPGASMKVSKASGYFTFNYYIHWRQAPGQGLEWMWINPNSGATNYAQKFQ</p> <p>GRVTMRDTSSTVYMEISSLRSEDYAVYCAKSWFASWGQTLVTVSSGGSGSGSGSGSG</p> <p>GSELVMTQSPDSLAVSLGERATINCKSSQSVLNSSNNRNYLAWYQKPGQPPLLIYWAISTRESG</p> <p>VPDRFSGSGSDFTLIISGLQAEDVAVYCCQHYSTPFTFGPTKVDIKSGSGGSSEVQLVESGG</p> <p>GLVQPGSLKLSCAASGFTFNYSAMNWRQAPGKLEWVARIRSKYNNYATYYADSVKGRFTISR</p> <p>DDSKNTAYLQMNILKTEDTAVYCVRHGNFGNSYVSWAYWGQTLVTVSSGGSGSGSGSGSG</p> <p>SQVVTQEPSTIVSPGTVTLTCSSTGAVTSGNYPNWQQKPGQAPRGLIGGTKFLAPGTPARF</p> <p>SGSLLGKKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGKLTIVL</p> <p>CAGGTGAGCTGGTCCAGTCTGGGCTGAGGTGAAGAGCCCTGGGCTCAATGAAGTCTCCTG</p> <p>CAAGGCTCTGGGTACACCTTCACCAACTACTATATACACTGGTGCAGACAGSCCCTGGACAAG</p> <p>GTCTTGAGTGGATGGTTGGATCAACCTAACAGTGGTGCACAACTATGCACAGAAGTCCAG</p> <p>GGCAGAGTCACCATGACCAGGGACACGTCCACGAGCACAGTCTACATGGAGTGAAGAGCTGAG</p> <p>ATCTGAGGACACGGCCGTGTATTACTGTGCGAAATCCTGGGTCTCCTGGTTTGTCTTGGGTC</p> <p>AAGGAACCTTGGTCAACCTCTCCTCAGGTGGTGGTGTCTGGCGGGGGCTCCGGTGGTGGT</p> <p>GGTCTGAGCTCGTATGACCCAGTCTCCAGACTCCCTGGTGTGTCTCTGGCGGAGAGGCGCAC</p> <p>CATCAACTGCAAGTCCAGCCAGAGTGTITTAACAGCTCCACAAATAGGAACACTAGCTTGGT</p> <p>ACCAGCAAAACCCAGGACAGCTCTTAAGTGTCTTACTGGCATCTACCCGGGAATCCGGG</p> <p>GTCCCTGACCGATTTCAGTGGCAGGGTCTGGGACAGATTCACTCTCACCATCAGTGGGCTGCA</p> <p>GGCTGAACATGTGGCAGTTTATTACTGTGCAACATATATAGTACTCCATTCACTTTGGCCCTG</p> <p>GGACCAAGTGGATATCAAAATCCGAGGTGGTGGATCCGAGGTGCAGTGGTGGATCTGGAGGA</p> <p>GGATTGGTGCAGCCTGGAGGTCAATGAACCTCTCATGTGCAGCCTCTGGATTCACTTCAATAG</p> <p>CTACGCCATGAACCTGGTCCGCCAGGTCCAGGAAAGGTTTGAATGGTGTGTCGCATAAGAA</p> <p>GTAATATAATAATAATTATGCAACATATTATGCCGATTCAGTGAAGGAGGTTCACCATCTCCAGA</p>	nt	artificial	<p>MCSP-G4 VH-VL-P</p> <p>x F12Q VH-VL</p>	<p>212.</p>

213.	MCSP-G4 VH-VL-P x 12C VH-VL	artificial	aa	<p>QVQLVQSGAEVKRPGASMKVSKASGVTFNTYIHWVRQAPQGLEWMGWINFNSGATNYAQKFQ GRVTRTDISTSTVYME LSSLRSEDTAVYYCAKSWVSWFASWGQGLVTVSSGGSGGGSGSGG GSELVMTQSPDSLAVSLGERATINCKSSQSVLNSSNRNLIWYQKPPKLLIYWASTSGG VPDRFSGSGTDFTLITISGLQAEIVAVYYCQOHYSTFTTFEFGPTKVDIKSGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAFGKLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAFLQMNHLKTEDTAVYYCVVRHGFNFSYISYWAYWGQGLVTVSSGGSGGGSGGGG SQTVVTEPSSLTVSPGGTVTLTSGSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKELAPGTPARF SGSLIGGKRAILTSLGVQPEDEAEYYICVLWYSNRVFEVGGIKLTVL</p>
214.	MCSP-G4 VH-VL-P x 12C VH-VL	artificial	nt	<p>CAGGTGCAGCTGGTCCAGTCTGGGCTGAGGTGAAGAGGCTGGGGCTCAATGAAGGTCTCCTG CAAGGCTTCTGGGTACACCTTCACCAACTACTATATACACTGGGTGCGACAGGCCCTGGACAAG GTCTTGAGTGGATGGTTGGATCAACCTAACAGTGTGCGACAAACTATGCACAAAGTCCAG GGCAGAGTCACCATGACCAGGGACAGTCCACGAGCACAGTACATGGAGTGCAGCAGCCTGAG ATCTGAGGACACGGCCGTGTATTACTGTGCGAAATCCTGGGTCTCTGGTTCCTGGTTCCTGGGTC AAGAACTTGGTCAACCTCTCCTAGTGGTGGTGGTCTGGCGGGGGGGCTCCGGTGGTGGT GGTCTGAGCTCGTGAIGACCCAGTCTCCAGACTCCCTGGTGTGTCTCTGGCGGAGAGGGCCAC CATCAACTGCAAGTCCAGCCAGAGTGTTTAAACAGCTCCAACTAGGAATCTAGCTTGGT ACCAGCAGAAACCAGGACAGCTCCTAAGCTGCTCATTTACTGGGCATCTACCGGGAATCCGGG GTCCCTGACCGATTTCAGTGGCAGCGGTCTGGGACAGATTTCACTCTCACCATCAGTGGCCTGCA GGCTGAAGATGTGGCAGTTTATTACTGCAGCAACATTAAGTACTCATTCATCTTGGCCCTG GGACCAAGTGGATATCAAA TCCGAGGTGGTGGATCCGAGGTGCAGCTGGTCGAGTCTGGAGGA GGATTGGTGCAGCCTGGAGGGTCATTGAACCTCTCATGTGCAGCCTCTGGATTCACCTTCAATAA GTACGCCATGAAC TGGTCCGCCAGGCTCCAGGAAAGGTTTGGAA TGGGTGCTCGCATAAAGAA GTAAATATAATAAT TATGCAACATATTATGCCGATTTCAGTGAAGACAGGTTTACCATCTCCAGA GATGATTCAAAAAACACTGCCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTA CTACTGTGAGACATGGGAAC TCCGTAATAGTACATCTCACTTGGGCTTACTGGGCCAAG GGACTGTGGTACCGCTCTCCTCAGTGGTGGTGGTTCTGGCGGGGGCTCCGGTGGTGGTGGT TCTCAGACTGTGTGACTCAGGAACCTTCACTCACCGTATCACTTGGTGGAACTCAGCTCAGCTCAC TTGTGGCTCCTCGACTGGGCTGTACATCTGGCACTACCAAACTGGGTCCCAAAAAACCAAG</p>

											<p>GTGAGCACCCCGTGGTCTAATAGTGGGACTAAGTTCTCGCCCCCGGTACTCTGCCAGATTCTCAGGCTCCCTGCTTGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGCAGAAATATTACTGTGTTCTATGTTACAGCAACCGCTGGTGTTCGGTGGAGAACCAACTACTGTCTCTA</p>
215.	MCSP-D2 VH-VL x H2C VH-VL	artificial	aa								<p>QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYMHVWRQAPQGLEWMGWINPNSGGTSYAQKFFQGRVTMRDSTSTVYMELSNLRSDTAVYCAKSWSWFASWGQGLTVTVSSGGSGGGSGGGGSDIVMTQSPDLSAVSLGERATINCKSSQSVLNSSNNRNYLAWYQQKPGQPPLLIYWAISTRESGVPDRFSGSGSTDFLTITISGLQAEDVAVYCOQHYSTFTFGPGTKVDIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNRLKTEDTAVYVCVRHGFNSYISYWAYWGQGLTVTVSSGGSGGGSGGGSGGGSQTVVTQEPSLTVSPGGTIVTLTCGSSTGAVTSGYYPNWVQKPGQAPRGLIGGTKFLAPGTPARFSGSLGGKAALTLSGVQPEDEAEYYCALWYSNRWVFGGCTKLTVL</p>
216.	MCSP-D2 VH-VL x H2C VH-VL	artificial	nt								<p>CAGGTGCAGCTGGTCCAGTCTGGGCTGAGGTCAAGAACCTGGGGCTCAGTGAAGGTCTCCTGCAGGCTCTGGATACACCTTCACCGGTACTATATGCACTGGTGGACAGGCCCTGGACAAGGGCTTGAAGTGGATGGATCAACCCCTAACAGCTGGTGGCACAAAGTCCACAGCAAGATCCAGGGCAGAGTCACCTAGCTAGGACACGTCCACGAGCACAGTCTACATGGAGCTGAGCAACCTGAGATCTGACGACACGGCCGTGATTACTGTGCGAAATCTCGGTCTCCTGGTTCCTTCCTGGGTCAAGAACTTGGTCACCGTCTCCTCAGGTGGTGGTCTTGGCGGGCGGCTCGGTGGTGGTGGTCTGTGATATCGTGATGACCCAGTCTCCAGACTCCTGGCTGTGTCTCTGGCGAGAGGCCACCATCAACTGCAAGTCCAGCCAGAGTGTTTAAACAGCTCCAACAATAGGAACACTACTAGCTGGTACCAGAGAAACCCAGGACAGCCTCCTAAGCTGCTCACTTACTGGGCATCTACCCGGGAAATCCGGGGTCCCTGACCGATTCAAGTGGCAGCGGTCTGGACACAGATTTCACTCTCACCATCACTGGCCCTGCAAGCTGAAGATGTGGCAGTTTATTACTGTCAAGCAACATATAGTACTCCATTCACTTTTGGCCCTGGACCAAAGTGGATATCAAAATCCGGAGGTGGTGGATCCGAGGTGCAGCTGGTCGAGTCTGGAGGGAATGGTGGTCAGCCTGGAGGGTCAATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAATTAAGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGGGTTTGAATGGTGTCTCGCATAAAGAAATAATAATAATAATGCAACATATATGCCGATTCAAGTGAAGACAGGTTCACTCTCCAGAGATTCAAAACACTGCCCTATCTACAAATGAACAACTTGAACACTGAGGACACTGCCGTGTACTGTGTGAGACATGGGAACCTCGGTATAGTACATATCTTACTGGCTTACTGGGGCAAGGGACTGTGGTCACCGTCTCCTCAGGTGGTGGTGTCTGGCGGGCGGCTCCGGTGGTGGTGGTTCTCAGACTGTGTGACTCAGGAACCTTCACTCACCCTATCACCTGGTGAACAGTCACTCACTTGTGGCTCCTCGACTGGGCTGTACATCTGGCTACTACCAAACTGGGTCCCAACAAAACCCAGGTCAGGACCCCGTGGTCTAATAGGTGGGACTAAGTTCCTCGCCCCGGTACTCTCTGCCAGATTCAGGCTCCCTGTGGAGGCAAGGTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAAGAAATATTACTGTGCTCTATGGTACAGCAACCGCTGGTGGTTCGGTGGAGGAACCAACTGACTGTCTCTA</p>
217.	MCSP-D2 VH-VL x	artificial	aa								<p>QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYMHVWRQAPQGLEWMGWINPNSGGTSYAQKFFQ</p>

<p>GRVTMTRDTSTSTVYMELSNLRSDDTAVYYCAKSWVSWFASWGQGLTVTVSSGGGGGGGGGGGGGGG GSDIVMTQSPDSLAVSLGERATINCKSSQSVLNSSNNRNLYAWYQKPGQPCKLLIYWASTRESG VPDRFSGSGGTDFLTITISGLQAEDEVYYCQHHYSTPFTFPGTKVDIKSGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNSYAMNWVRQAPGKLEWVARIRSKYNNYATYYADSVKGRFTISR DDSKNTAYLQMNLLKTEDTAVYYCVRHGNEFNSYVSWWAYWGQGLTVTVSSGGGGGGGGGGGGG SQTVVTEPESLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQKPGQAPRGLIGGTKFLAPGTPARF SGSLLGGKAALTISGVQPEDEAEYYCVLWYSNRWVFGGKLTIVL</p>	<p>CAGGTGCAGCTGGTCCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAGTGAAGGTCTCCTG CAAGGCTTCTGGATACACCTTCACCGGCTACTATATGCACTGGTGGACAGGCCCTGACACAAG GGCTTGAGTGGATGGATCAACCTAACAGTGGTGACACAGCTACATGGAGCTGAGCAACCTGAG GGCAGAGTCACCAATGACTAGGACACGTCCAGAGACACAGTCTCCTGGTCTCCTGGTTCCTGGGT ATCTGACGACACGGCCGTCTCCTCAGGTGGTGGTCTGGCGGGCGGCTCCGGTGGTGGT AAGGAACCTTGGTCAACCTCTCCTCAGGTGGTGGTCTGGCGGGCGGCTCCGGTGGTGGT GGTCTGATATCGTGTGACCCAGTCTCCAGACTCCCTGGTGTGTCTCTGGCGGAGAGGCCAC CATCAACTGCAAGTCCAGCCAGAGTGTAAACAGCTCAACATAGGAACACTAGCTTGGT ACCAGCAGAAACCAGGACAGCCTCCTAAGCTCTCATTACTGGGCATCTACCCGGGAATCCGGG GTCCCTGACCGATTTCAGTGGCAGCGGCTGGGACAGATTCTACTCACCATCAGTGGCCTGCA GGCTGAAGATGTGGCAGTTTATTACTGTGCAACATATAGTACTCATTCACTTTGGCCCTG GGACCAAAGTGGATATCAATCCGGAGGTGGTGGATCCGAGGTGAGCTGGTGGTGGTGGTGGT GGATTGGTGACGCTGGAGGTCAATTGAACCTCTCATGTGACGCTCTGGATTCACTTCAATAG CTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAGGTTTGAATGGTGTCTCGCATAGAA GTAATATATAATATATGCAACATATTATGCCGATTTCAGTGAAGGAGGTTTCAACATCTCCAGA GATGATTCAAAAACACTGCCTATCTACAAATGAACAACTTGAAACTGAGGACACTGCCGTGTA CTACTGTGTGAGACATGGAACTTCGGTAATAGCTACGTTTCTGGTGGCTTACTGGGGCCAAAG GGAATCTGGTCAACCGTCTCCTCAGGTGGTGGTCTGGCGGGCGGCTCCGGTGGTGGTGGT TCTCAGACTGTGTGACTCAGGAACCTTCACTACCGTATCACCTGGTGGACAGTCACTCAC TTGTGGCTCCTCGACTGGGCTGTACATCTGGCAACTACCAAACTGGTCCAAACAAACCCAG GTCAGGCACCCGTTGTTCTAATAGGTGGACTAAGTCTCTCGCCCCGTACTCTGCGCAGATT TCAGGCTCCCTGCTTGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGC AGAATATTACTGTGTTCTATGTTACAGCAACCGCTGGGTGTTCTGGTGGAGGAACCAAACTGACTG TCCTA</p>
<p>218.</p>	<p>MCSP-D2 VH-VL x F12Q VH-VL</p> <p>artificial</p> <p>nt</p>
<p>219.</p>	<p>MCSP-D2 VH-VL x I2C VH-VL</p> <p>artificial</p> <p>aa</p>

220.	MCSP-D2 VH-VL x I2C VH-VL	artificial	nt	<p>SQFVVTQEPSTLTVSPGGTGTTLTCSSTGAVTSGNYPNWVQKPGQAPRGLIGGTRKFLAPGTPARF SGSLLGGKAAALTLSGVQPEDEAEYYCVLWYSNRWVFGGTKLTVL</p> <p>CAGGTGACGCTGGTCCAGTCTGGGGCTGAGTGAAGAAGCCTGGGGCTCAGTGAAGGTCTCCTG CAAGGCTTCTGGATACACCTTCAACGGCTACTATATGCACTGGTGGACAGGCCCTGGACAAG GGCTTGAAGTGGATGGATGATCAACCTAACAGTGGTGGACAAAGCTACGCACAGAAGTTCAG GGCAGAGTCACCACTAGTAGGACACGTCACGACGACACACTTACATGGAGCTGAGCAACTGAG ATCTGACGACACGGCCGTGTATTACTGTGCGAAATCCTGGGTCTCCTGGTTTCTCTGGGTG AAGGAACCTTGGTCAACGCTCTCTCAGTGGTGGTGTCTGGCGGGGGCTCCGGTGGTGGT GGTCTGATATCGTGTGATGACCCAGTCTCCAGACTCCCTGGCTGTGTCTCTGGCGAGAGGCCAC CATCAACTGCAAGTCCAGCCAGAGTGTCTTAAACAGCTCAACAATAGGAACACTAGCTTGGT ACCAGAGAAACAGGACAGCCTCTAAGCTGCTCATTTACTGGCATCTACCCGGGAATCCGGG GTCCCTGACCGATTTCAGTGGCAGGGTCTGGACAGATTTCATCTCAACATCAGTGGCTGCA GGCTGAAGATGTGGCAGTTTATTACTGTGACCAACATATAGTACTCCATTCACTTTGGCCCTG GGACCAAGTGGATATCAATCCGGAGGTGGTGGATCCGAGGTGAGTCTGATTCAGCTTCACTTCAATAA GGATTGGTGACGCTGGAGGTCTTGAACCTCTCATGTGAGCTCTGATTCACCTTCAATAA GTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGGTTTGAATGGTTGCTCGCATAAAGAA GTAAATATAATAATTATGCAACATATTATGCCATTTCAGTGAAGACAGGTTCCACATCTCCAGA GATGATTCAAAACACTGCCTATCTACAAATGAACAACTTGAACACTGAGGACACTGCCGTGTA CTACTGTGTGAGACATGGGAACCTTCGGTAACTAGTACATATCTACTGGCTTACTGGGCCAAG GGACTGTGTCACCGTCTCCTCAGGTGGTGGTGTCTGGCGGGGGCTCCGGTGGTGGTGGT TCTCAGACTGTGTGACTCAGGAACCTTCACTACCGTATCACCTGGTGAACAGTCACTCAC TTGTGGCTCCTCGACTGGGCTGTACATCTGCAACTACCCAACTGGTCCCAACAAAACCCAG GTCAGGCACCCCGTGGTCTAATAGGTGGGACTAAGTTCTCCGCCCGGTACTCCTGCCAGATTCTC TCAGGCTCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGC AGAAATATTACTGTGTCTATGTTACAGCAACCCGCTGGGTGTTCGGTGGAGGAACCAACTGACTG TCCTA</p>
221.	MCSP-D2 VH-VL-P x H2C VH-VL-P	artificial	aa	<p>QVQLVQSGAEVKKPGASVKVSKASGYTFTGYMHWVRQAPQGLEWMGWINPNSCGTSYAQKFQ GRVTMTRDTSTSTVYMELSNLRSDDTAVYCAKSWVSWFASWGQGLTVTVSSGGSGSGSGGG GSELVMTQSPDLSAVSLGERATINCKSSQSVLNSNNRNLYAWYQKPGQPPKLLIYWASTRESG VPDRFSGSGSDFTLTISGLQAEDEVAVYCOQHSTPFTFGPTKVDIKSGGGSEVQLLES GLVQPGGSLKLSCAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNLLKTEDTAVYCVRHGNFNSYISYWAYWGQGLTVTVSSGGSGSGSGGGGG SELVVTQEPSTLTVSPGGTGTTLTCSSTGAVTSGNYPNWVQKPGQAPRGLIGGTRKFLAPGTPARF SGSLLGGKAAALTLSGVQPEDEAEYYCVLWYSNRWVFGGTKLTVL</p>
222.	MCSP-D2 VH-VL-P x H2C VH-VL-P	artificial	nt	<p>CAGGTGACGCTGGTCCAGTCTGGGGCTGAGTGAAGAAGCCTGGGGCTCAGTGAAGGTCTCCTG CAAGGCTTCTGGATACACCTTCAACGGCTACTATATGCACTGGTGGACAGGCCCTGGACAAG GGCTTGAAGTGGATGGATGATCAACCTAACAGTGGTGGCACAAGCTACGCACAGAAGTTCACAG</p>

<p>GGCAGAGTCACCATGACTAGGGACACGTCACGAGCACAGTCTACATGGAGCTGAGCAACCTGAG ATCTGACGACACAGCGCGTGTATTACTGTGCGAAATCCTGGGTCTCCTGGTTTGGTTCCTGGGTC AAGAACTTGGTCACCGTCTCCTCAGGTGGTGGTCTTGGCGGGCGGCTCCGGTGGTGGT GGTCTGAGCTCGTATGACCCAGTCTCCAGTCCCTGAGTCCCTGGTGTGTCTCTGGCGGAGAGGGCAC CATCAACTGCAAGTCCAGCCAGAGTGTAAACAGCTCCAACAATAGAACTACTTGGTGGT ACCAGAGAAACAGGACAGCCTCCTAAGTGTCTTACTGGCATCTACCCGGGAAATCCGGG GTCCCTGACCGATTGAGTGGCAGGCTGAGGACAGATTTCACTCTCACCATCAGTGGCTGCA GGCTGAAGATGTGGCAGTTTACTGTGAGCAACATTATAGTACTCATTCACTTTTGGCCCTG GGACCAAGTGATATCAATCCGAGGTGGTGGATCCGAGGTGAGTCTGCTGAGTCTGAGGA GGAATGGTGACGCTGAGGGTCAATGAACTCTCATGTGAGCCTCTGGATTCACTTCAATAA GTACGCCATGAACCTGGTCCGCCAGGCTCCAGAAAGGTTTGAATGGTGTCTGCTGCAAGAA GTAAATATAAATAATTGCAACATATTGCGGATTCAGTGAAGACAGGTTCACTCTCCAG GATGATTCAAAAACACTGCCTATCTACAAATGAACAACTTGAACACTGAGGACACTGCCGTGTA CTACTGTGAGACATGGGAATTCGGTAACTAGCTACATATCTTCTGCGCTTACTGGGCGCAAG GGACTGTGGTCAACGCTCTCCTCAGGTGGTGGTCTTGGCGGGCGGCTCCGGTGGTGGTGGT TCTGAGCTCGTTGTGACTCAGGAACCTTCACTACCGTATCACCTGGTGAACAGTCACTCAC TTGTGGTCTCTGACTGGGCTGTACATCTGGTACTACCAAACTGGTCCAAACAAAACAG GTCAGGACACCGTGGTCTAATAGTGGGACTAAGTCTCTGCCCCGCTACTCTGCTGAGATT TCAGCTCCCTGCTTGGAGGCAAGCTGCCCTCACCTCTCAGGCTACAGCCAGAGATGACGC AGAAATATTACTGTGCTCTATGGTACAGCAACCGCTGGTGGTTCGGTGGAGAACCAACTGACTG TCCTA</p>			
<p>223.</p>	<p>MCSP-F9 VH-VL x H2C VH-VL</p>	<p>artificial</p>	<p>aa</p>
<p>224.</p>	<p>MCSP-F9 VH-VL x H2C VH-VL</p>	<p>artificial</p>	<p>nt</p>

114

115

229.	1-27 CD3ε-Fc	artificial	aa	<p>TCTGAGCTCGTTGTGACTCAGGAACCTTCACTCACCGTATCACCTGGTGAACAGTCACACTCAC TTGTGGCTCCTCGACTGGGGCTGTTACATCTGGCTACTACCAAACTGGTCCCAAAAAACACAG GTCAGGCACCCCGTGGTCTAATAGGTGGACTAAGTCTCCTGCCCGGTACTCCTGCCAGATTCT TCAGGCTCCCTGCTTGGAGGCAAGGTCCTCACCCTCTCAGGGGTACAGCCAGGATGAGGC AGAAATATTACTGTGCTCTATGGTACAGCACCGCTGGGTGTTCCGGTGGAGGAACCAAACTGACTG TCCTA</p> <p>QDQNEEMGGITQTPYKVSISGTTVILTSCEPKSCDKTHTCPPAPPELLGGPSVFLFPPKPKDTL MI SRTPEVTCVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYCKKVSNAKALPAPIEKTIISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEW ESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPG KHHHHH</p> <p>ATGGGATGAGCTGTATCATCCTCTTCTGGTAGCAACAGCTACAGGTGTACACTCCCAAGATGG TAAATGAAGAAATGGGTGGTATTACACAGACACCATATAAAGTCTCCATCTCTGGAACACAGTAA TATTGACATCCGGAGAGCCCAATCTTGTGACAAACTCACACATGCCACCGTCCCGACGACCT GAACTCCTGGGGGACCGTCAGTCTTCTCTCCCCCAAAACCCAGGACACCTCATGATCTC CCGACCCCTGAGGTCACATGCGTGGTGGTGGACGTGAGCCACGAAGACCTGAGGTCAAGTTCA ACTGGTACGTGGACGGCTGGAGGTGCTAATGCCAAGACAAAGCCGGGAGGAGGAGTACAAC AGCAGTACCGTGTGGTCAAGTCTCCTGCTGACAGGACTGAGTGAATGCAAGGAGTA CAAGTGCAAGGTCTCCAAACAAAGCCCTCCAGCCCTCCAGGAGGAGTATCCCAAGCCAAAG GGCAGCCCGAGAACACAGGTGTACACCTCCCGCTCCCGGAGGAGTACCCAGAACACAG GTCAGCTGACCTGCTGGTCAAGGCTTCTATCCAGCGACATCCCGTGGAGTGGAGAGCA TGGCAGCCGGAGAACAACTACAAGACCCGCTCCGCTGCTGACTCCGACGGCTCCTCTCTCC TCTATAGCAAGCTCACCGTGGACAGAGCAGGTGGCAGAGGGAACGCTCTTCTCATGCTCCGTG ATGCATGAGGCTCTGCACAACTACACGAGAGAGGCTCTCCCTGTCCCCGGGTAAACATCA TCACATCATCAT</p> <p>QDQNEEMGGITQTPYKVSISGTTVILTDYKDDDKTASFAAAQKEVCENYKLVNCFINDNGQC QCTSIGAQTIVLCSKLAAKCLVMKAEEMNGSKLGRAPKEGALQNDGLYDPDCDESGLEKAKQCN GTSTCWCNTAGVRRTDKDEITCSERVITYWIIELKHKAREKPYDVQSLRTALEEAIKTRYQL DPKFTNIIYEDNVTIDLVQNSSQKTQNDVDIADVAYVYFEKDVKGESLFHSKMDLRVNGEQLD LDPGQTIIYYVDEKAPEFSMQGLKAGVIAIVVWVIAIVAGIWLVI SRKRMAKYEKAEIKEMG EMHREINA</p> <p>ATGGGATGAGCTGTATCATCCTCTTCTGGTAGCAACAGCTACAGGTGTACACTCCCAAGATGG TAAATGAAGAAATGGGTGGTATTACACAGACACCATATAAAGTCTCCATCTCTGGAACACAGTAA TATTGACAGATTACAAGGACGAGGTGACAGACTGCGAGTGTGGCCGAGCTCAGAAAGATGT GTCTGTGAAAACACTACAAGCTGGCCGTAACTGCTTTTGAATGACAAATGGTCAATGCCAGTGTAC TTCGATTGGTGCAAAAATACTGTCTTCTTCTCAAGCTGGCTGCCAAATGTTTGGTGTATGAAGG CAGAAATGAACGGCTCAAACTTGGGAGAGAGGCAACCTGAAGGGGCTCTCCAGAACCAATGAT</p>
230.	1-27 CD3ε-Fc	artificial	nt	
231.	human 1-27 CD3ε - EpCAM	artificial	aa	
232.	human 1-27 CD3ε - EpCAM	artificial	nt	

				<p>GGCTTTACGATCCTGACTGCGATGAGAGGGGCTCTTTAAGCCAAAGCAGTGCACGGCACTC CACGTGCTGGTGTGTGAACACTGCTGGGTGAGAACTGACAAAGGACACTGAAATAACCTGCT CTGAGCGAGTGAGAACTTACTGATCATCATTAATTAATAACAAAGCAAGAGAAAACTTAT GATGTTCAAAGTTTGGGACTGCACTTGAGGAGCGATCAAAACCGGTTATCAACTGGATCCAAA ATTATCACAAATATTTTGTATGAGGATAATGTTATCACTATTGATCTGGTTCAAATCTTCTC AGAAAACTCAGAAATGATGTGGACATAGCTGATGGCTTATTTTGAAGAGATGTTAAAGT GAATCCTTGTTCATTTCAATAAGAAATGGACCTGAGAGTAAATGGGAACAACCTGGATCC TGGTCAAACTTTAATTTATTTATGTCGATGAAAAAGCACCTGAATCTCAATGCAGGGTAAAG CTGGTATTGCTGTTATTGTTGTTGTCATAGCAATTTGCTGGAATTTGTTGCTGGT ATTCCAGAAAGAGAAATGGCAAGTATGAGAAAGCTGAGATAAAGGAGATGGGTGAGATGCA TAGGAACTCAATGCA</p>
233.	marmoset 1-27 CD3ε -EpCAM	artificial	aa	<p>QDGNEEMGDTTQNPYKVISGTTVTLLTDYKDDDKTASFAAAQKEVCVCENYKLVNCFLNNGQC QCTSIGAONTVLCSKLAACKLVKAEEMNGSKLGRRAKPEGALQNNDGLYDPCDESGLEFKAKQCN GTSTCWCVNTAGVRRTDKDEITCSERVITYWIIELKHKAREKPYDVQSLRTALEEAIKTRYQL DPKFTINILYEDNVITIDLQNSSQKTQNDVDIADVYYFEKDVKGESLFHSKKMDLRVNGEQLD LDPGQTLIIYYVDEKAPEFSMQGLKAGVIAIVVVVIAIVAGIVVLVISRKRMAKYEKAEIKEMG EMHREINA</p>
234.	marmoset 1-27 CD3ε -EpCAM	artificial	nt	<p>ATGGGATGGAGCTGTATCATCCTCTTCTTGTAAGCAACAGCTACAGGTGTACCTCCAGGACGG TAATGAAGAAATGGGTGATACACAGAAACCATATAAAGTTTCCATCTCAGGAACACAGTAA CACTGACAGATTACAAGGACGAGTACAAAGTCTGCGAGTTTCCCGCAGCTCAGAAAGAAATGT GTCTGTGAAAACCTACAAGCTGGCCGTAACTGCTTTTGAATGACAAATGGTCAATGCCAGTGTAC TTCGATTGGTGCAAAATACTGCTCTTGTCTCAAAGCTGGTCCAAATGTTTGGTGATGAAGG CAGAAATGAACGGCTCAAAACTTGGGAGAGAGCGAAACCTGAAGGGCTCTCCAGAACAAATGAT GGCCTTTACGATCCTGACTGCGATGAGAGCGGCTCTTTAAGGCCAAGCAGTGCACCGGACCTC CACGTGCTGGTGTGAACACTGCTGGGTGAGAAAGTACAAAGGACACTGAAATAACCTGCT CTGAGCGAGTGAGAACCTACTGGATCATCATTAATAAACAAGAGAGAAAAACCTTAT GATGTTCAAAGTTTGGGACTGCCTTGAGAGCGGATCAAAACGGTTATCAACTGGATCCAAA ATTTATCACAAATATTTTGTATGAGGATAATGTTATCACATTGATCTGGTTCAAATCTTCTC AGAAAACTCAGAAATGATGTGGACATAGCTGATGGCTTATTTTGAAGAGATGTTAAAGT GAATCCTTGTTCATTTCAATAAGAAATGGACCTGAGAGTAAATGGGAACAACCTGGATCC TGGTCAAACTTTAATTTATTTATGTCGATGAAAAAGCACCTGAATCTCAATGCAGGGTAAAG CTGGTATTGCTGTTATTGTTGTTGTCATAGCAATTTGCTGGAATTTGTTGCTGGT ATTCCAGAAAGAGAGAAATGGCAAGTATGAGAAAGCTGAGATAAAGGAGATGGGTGAGATGCA TAGGAACTCAATGCA</p>
235.	tamarin 1-27 CD3ε - EpCAM	artificial	aa	<p>QDGNEEMGDTTQNPYKVISGTTVTLLTDYKDDDKTASFAAAQKEVCVCENYKLVNCFLNNGQC QCTSIGAONTVLCSKLAACKLVKAEEMNGSKLGRRAKPEGALQNNDGLYDPCDESGLEFKAKQCN GTSTCWCVNTAGVRRTDKDEITCSERVITYWIIELKHKAREKPYDVQSLRTALEEAIKTRYQL</p>

55	236.	tamarin 1-27 CD3ε - EpCAM	artificial	nt	<p>DPKFI TNILYEDNVITIDL VQNSSQKTQNDVDIADVAYYFEKDVKGESLFHSHKMDLRVNGEQLD LDPGQTLIIYYVDEKAPEFSMQGLKAGVIAIVVVVIAIVAGIVVLVLSRKRMAYEKAEIKEMG EMHREINA</p> <p>ATGGGATGGAGCTGTATCATCCTCTCTTGTGAGCAACAGCTACAGGTGTACACTCCCAGGACGG TAATGAAGAAATGGGTGATACACAGAACCCATATAAAGTTTCCATCTCAGGAACACAGATAA CACTGACAGATTACAAGGACGAGATGACAGACTGCGAGTTTTCGCCAGCTCAGAAAAGATGT GTCTGTGAAAACACAAAGCTGGCCGTAACTGCTTTTGAATGACAAATGGTCAATGCCAGTGTAC TTCGATTGGTGACAAAATACTGTCTTTGCTCAAGCTGGTCCAAATGTTTGGTGTGAAGG CAGAAATGAACGGCTCAAACTTGGGAGAGAGCGAAACCTTAAGGCCAAGCAGTSCAACGGCACCTC GGCTTTACGATCCTGACTGCGATGAGAGCGGGCTTTAAGGCCAAGCAGTSCAACGGCACCTC CACGTGCTGGTGTGAACACTGCTGGGTGAGAGAACTGACAAAGGACACTGAAATAACCTGCT CTGAGCGAGTGAGAACCTACTGGATCATATTGAATTAACAACAAGCGCTTATCAACTGGATCCAAA GATGTTCAAAGTTTGGGACTGCACCTGAGGAGCGGATCAAAACGCTTATCAACTGGATCCAAA ATTATCACAAATATTTTGTATGAGGATAATGTATCACTATTGATCTGGTTCAAAATCTCTCTC AGAAAACACAGAAATGATGTGACATAGCTGATGCTGCTTATTTTGAAGAAAGATGTTAAAGT GAATCCTTGTTCATTTCAATTAAGAAATGGACCTGAGAGTAAATGCGGACAACTGATCC TGCTCAAACTTTAATTTATATGTCGATGAAAACGACCTGAGAGTAAATGCGGACAACTGATCC CTGGTGTATTGCTGTTATTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTTGTT ATTCCAGAAAAGAGAGATGGCAAGTATGAGAAAGCTGAGATAAAGGAGATGGGTGAGATGCA TAGGGAACCTCAATGCA</p> <p>QDNEEIGDTONPYKVISGTTVTLTDYKDDDDKTASFAAQKEVCENYKLVNCFIINDNGQC QCTSIGAONTVLCSKLAACKLVKMAEMNGSKLGRRAKPEGALQNDGLYDPDCDESGLEKAKQCN GTSTCWCVNTAGVVRTDKDTEITCSERVITYWIIELKHKAREKPYDVQSLRTALEEAIKTRYQL DPKFI TNILYEDNVITIDL VQNSSQKTQNDVDIADVAYYFEKDVKGESLFHSHKMDLRVNGEQLD LDPGQTLIIYYVDEKAPEFSMQGLKAGVIAIVVVVIAIVAGIVVLVLSRKRMAYEKAEIKEMG EMHREINA</p> <p>ATGGGATGGAGCTGTATCATCCTCTCTTGTGAGCAACAGCTACAGGTGTACACTCCCAGGACGG TAATGAAGAGATTGGTGATACACCCAGAACCCATATAAAGTTTCCATCTCAGGAACACAGATAA CACTGACAGATTACAAGGACGAGATGACAGACTGCGAGTTTTCGCCAGCTCAGAAAAGATGT GTCTGTGAAAACACAAAGCTGGCCGTAACTGCTTTTGAATGACAAATGGTCAATGCCAGTGTAC TTCGATTGGTGACAAAATACTGTCTTTGCTCAAGCTGGTCCAAATGTTTGGTGTGAAGG CAGAAATGAACGGCTCAAACTTGGGAGAGAGCGAAACCTTAAGGCCAAGCAGTSCAACGGCACCTC GGCTTTACGATCCTGACTGCGATGAGAGCGGGCTTTAAGGCCAAGCAGTSCAACGGCACCTC CACGTGCTGGTGTGAACACTGCTGGGTGAGAGAACTGACAAAGGACACTGAAATAACCTGCT CTGAGCGAGTGAGAACCTACTGGATCATATTGAATTAACAACAAGCGCTTATCAACTGGATCCAAA GATGTTCAAAGTTTGGGACTGCACCTGAGGAGCGGATCAAAACGCTTATCAACTGGATCCAAA ATTATCACAAATATTTTGTATGAGGATAATGTATCACTATTGATCTGGTTCAAAATCTCTCTC</p>
40	237.	squirrel monkey 1-27 CD3ε -EpCAM	artificial	aa	<p>QDNEEIGDTONPYKVISGTTVTLTDYKDDDDKTASFAAQKEVCENYKLVNCFIINDNGQC QCTSIGAONTVLCSKLAACKLVKMAEMNGSKLGRRAKPEGALQNDGLYDPDCDESGLEKAKQCN GTSTCWCVNTAGVVRTDKDTEITCSERVITYWIIELKHKAREKPYDVQSLRTALEEAIKTRYQL DPKFI TNILYEDNVITIDL VQNSSQKTQNDVDIADVAYYFEKDVKGESLFHSHKMDLRVNGEQLD LDPGQTLIIYYVDEKAPEFSMQGLKAGVIAIVVVVIAIVAGIVVLVLSRKRMAYEKAEIKEMG EMHREINA</p> <p>ATGGGATGGAGCTGTATCATCCTCTCTTGTGAGCAACAGCTACAGGTGTACACTCCCAGGACGG TAATGAAGAGATTGGTGATACACCCAGAACCCATATAAAGTTTCCATCTCAGGAACACAGATAA CACTGACAGATTACAAGGACGAGATGACAGACTGCGAGTTTTCGCCAGCTCAGAAAAGATGT GTCTGTGAAAACACAAAGCTGGCCGTAACTGCTTTTGAATGACAAATGGTCAATGCCAGTGTAC TTCGATTGGTGACAAAATACTGTCTTTGCTCAAGCTGGTCCAAATGTTTGGTGTGAAGG CAGAAATGAACGGCTCAAACTTGGGAGAGAGCGAAACCTTAAGGCCAAGCAGTSCAACGGCACCTC GGCTTTACGATCCTGACTGCGATGAGAGCGGGCTTTAAGGCCAAGCAGTSCAACGGCACCTC CACGTGCTGGTGTGAACACTGCTGGGTGAGAGAACTGACAAAGGACACTGAAATAACCTGCT CTGAGCGAGTGAGAACCTACTGGATCATATTGAATTAACAACAAGCGCTTATCAACTGGATCCAAA GATGTTCAAAGTTTGGGACTGCACCTGAGGAGCGGATCAAAACGCTTATCAACTGGATCCAAA ATTATCACAAATATTTTGTATGAGGATAATGTATCACTATTGATCTGGTTCAAAATCTCTCTC</p>
45	238.	squirrel monkey 1-27 CD3ε -EpCAM	artificial	nt	<p>QDNEEIGDTONPYKVISGTTVTLTDYKDDDDKTASFAAQKEVCENYKLVNCFIINDNGQC QCTSIGAONTVLCSKLAACKLVKMAEMNGSKLGRRAKPEGALQNDGLYDPDCDESGLEKAKQCN GTSTCWCVNTAGVVRTDKDTEITCSERVITYWIIELKHKAREKPYDVQSLRTALEEAIKTRYQL DPKFI TNILYEDNVITIDL VQNSSQKTQNDVDIADVAYYFEKDVKGESLFHSHKMDLRVNGEQLD LDPGQTLIIYYVDEKAPEFSMQGLKAGVIAIVVVVIAIVAGIVVLVLSRKRMAYEKAEIKEMG EMHREINA</p> <p>ATGGGATGGAGCTGTATCATCCTCTCTTGTGAGCAACAGCTACAGGTGTACACTCCCAGGACGG TAATGAAGAGATTGGTGATACACCCAGAACCCATATAAAGTTTCCATCTCAGGAACACAGATAA CACTGACAGATTACAAGGACGAGATGACAGACTGCGAGTTTTCGCCAGCTCAGAAAAGATGT GTCTGTGAAAACACAAAGCTGGCCGTAACTGCTTTTGAATGACAAATGGTCAATGCCAGTGTAC TTCGATTGGTGACAAAATACTGTCTTTGCTCAAGCTGGTCCAAATGTTTGGTGTGAAGG CAGAAATGAACGGCTCAAACTTGGGAGAGAGCGAAACCTTAAGGCCAAGCAGTSCAACGGCACCTC GGCTTTACGATCCTGACTGCGATGAGAGCGGGCTTTAAGGCCAAGCAGTSCAACGGCACCTC CACGTGCTGGTGTGAACACTGCTGGGTGAGAGAACTGACAAAGGACACTGAAATAACCTGCT CTGAGCGAGTGAGAACCTACTGGATCATATTGAATTAACAACAAGCGCTTATCAACTGGATCCAAA GATGTTCAAAGTTTGGGACTGCACCTGAGGAGCGGATCAAAACGCTTATCAACTGGATCCAAA ATTATCACAAATATTTTGTATGAGGATAATGTATCACTATTGATCTGGTTCAAAATCTCTCTC</p>

55					<p>AGAAACTCAGAAUGATGTGGACATAGCTGATGTGGCTTATATTTTGAAAAAGATGTTAAAGGT GAATCCTTGTTCATCTAAGAAAAATGGACCTGAGAGTAATAATGGGAACAACCTGGATCTGGATCC TGGTCAAACTTTAAATTTATATGTCGATGAAAAAGCACCTGAATCTCAATGCAGGGTCTAAAAAG CTGGTGTATTGCTGTATTGTTGTTGTTGATAGCAATTTGCTGGAATTTGCTGCTGGTT ATTCCAGAAAAGAGAGAAATGGCAAAGTATGAGAAAGGCTCAGATAAAGGAGATGGGTGAGATGCA TAGGGAACCTCAATGCA</p>
239.	swine 1-27 CD3ε - EpCAM	artificial	aa		<p>QEDIERPDEDQTKFKVISGDKVELTDYKDDDDKTASFAAAQKEVCENYKLVNCFINDNGQC QCTSIGAONTVLCSKLAACKLVKMAEMNGSKLRRRAKPEGALQNDGLYDPDCDESGLEKAKQCN GTSTCWCNTAGVRRTDKDEITCSERVITYWIIELKHAREKPYDVQSLRTALEEAIKTRYQL DPKFITNILYEDNVIITIDLQNSSQKTQNDVDIADVAIFYFEKDVKGESLFHSHKMDLRVNGEQLD LDPGQTLIYYVDEKAPFESMQGLKAGVIAIVVVVIAIVAGIVVVIISRKRMAYEKAEIKEMG EMHRELNA</p>
240.	swine 1-27 CD3ε - EpCAM	artificial	nt		<p>ATGGGATGGAGCTGTATCATCTCTCTTCTGGTAGCAACAGCTACAGGTGTACATCCCAAGAAGA CATTGAAAGACCCAGATGAAGATACACAGAAAACATTTAAAGTCTCCATCTCTGGAGACAAGTAG AGCTGACAGATTACAAGGACGACGATGACAAGACTGCCAGTTTGGCCGAGCTCAGAAAGAAATGT GTCGTGAAAACACTACAAGCTGGCCGTAACTGCTTTTGAATGACAATGGTCAATGCCAGTGTAC TTCGATTGGTGCACAAAATACTGTCTCTTGTCTCAAAGCTGGCTGCCAAATGTTTGGTGATGAAGG CAGAAATGAACGGCTCAAAACTTGGGAGAGAGCGAAACCTGAAGGGCTCTCCAGAAACAATGAT GGCCTTTACGATCCTGACTGCGATGAGAGCGGGCTCTTAAAGCCAAAGAGTGAACGGGACCTC CACGTGCTGGTGTGAACACTGCTGGGGTCAGAAAGACTCAGAAAGACACTGAAATAACCTGCT CTGAGCGAGTGAGACCTACTGGATCATCATTTGAATTTAAACACAAAGCAAGAGAAAAACCTTAT GATGTTCAAAGTTTGGCGACTGCACCTGAGGAGCGGATCAAAACCGCTTATCAACTGGATCCAAA ATTTATCACAAATATTTGTATGAGGATAATGTTATCACTATTGATCTGGTTCAAAATCTCTCTC AGAAACTCAGAAATGATGTGGACATAGCTGATGTGGCTTATTTTGAAAAAGATGTTAAAGGT GAATCCTTGTTCATCTAAGAAAAATGGACCTGAGAGTAAATGGGGAACAACCTGGATCTGGATCC TGGTCAAACCTTTAATTTATATGTCGATGAAAAAGCACCTGAATTTCTCAATGCAGGGTCTAAAAAG CTGGTGTATTGCTGTATTGTTGTTGTTGATAGCAATTTGCTGGAATTTGTTGCTGGTT ATTTCCAGAAAAGAGAGAAATGGCAAAGTATGAGAAAGGCTCAGATAAAGGAGATGGGTGAGATGCA TAGGGAACCTCAATGCA</p>
241.	human CD3 epsilon chain	human	aa		<p>QDNEEMGGITQTTPYKVISGTTVILTCPPQYPSGSELLWHDNDKNIIGDEDDKNIIGSEDEHLSLKE FSELEQSGYVYCPYPRGSKPEDANFYLYLRARVCENCMEMDMVSVATIVIVICITGGLLLLVYYW SKNRKAKAKPVTRGAGGQRQGNKRPVPPVNPDIPIRKQORDLYSGLNQRRI</p>
242.	human CD3 epsilon chain	human	nt		<p>ATGCAGTCGGGCACTCACTGGAGAGTTCTGGCCCTCTGCCCTTATCAGTTGGCGTTTGGSGGCA AGATGGTAATGAAGAAATGGGTGGTATTACACAGACACCATATAAAGTCTCCATCTCTGGAAACA CAGTAATATTGACATGCCCTCAGTATCCTGGATCTGAATACTATGGCAACACAAATGATAAAAC ATAGGCGGTGATGAGGATGATAAAACATAGGCAGTATGAGGATCACCTGTCTACTGAAGGAATT TTCAGAAATTGGAGCAAAAGTGTATTATGTCTGTCTACCCAGAGGAAGCAACACAGAAAGATGCGA</p>

				ACTTTATCTCTACCTGAGGCGACGGGTGTGTGAGAACTGCATGGAGATGGATGTGATGTCGGTG GCCACAAATTGTACATAGTGGACATCTGCATCACTGGGGCTTGTCTGCTGTTTACTACTGAG CAAGAAATAGAAAGGCCAAGGCCAAGCCTGTGTGACAGGAGCGGGTGTGGCGGAGCAAGGG GACAAAACAAGGAGAGGCCACCACTGTTCCTCCAAACCCAGACTATGAGCCCATCCGGAAAGGCCAG CGGACCTGTATTCTGGCCTGAATCAGAGACGCATC MGWSCIIILFLVATATGVHS
243.	19 amino acid immunoglobulin leader peptide	artificial	aa	ATGGATGGAGCTGTATCATCTCTTCTTGTAGCAACAGCTACAGGTGTACACTCC
244.	19 amino acid immunoglobulin leader peptide	artificial	nt	AKTTPPSVYPLAPGSAQNSMVTGLCLVKGYPEPVTVTWNSGSLSSGVHTFPAVLQSDLYTLS SSVTVPSSTWPSSETVTCNVAHPASSTKVDKKIVPRDCGCKPCICTVPEVSSVFIFFPKPKDVLTI TLTPKVTGVVDISKDDPEVQFSWFVDDEVHTAQTPREEQNFSTRVSSELPIMHQDWLNGKE FKCRVNSAAFPAPIEKTISKTKGRPKAPQVYTIIPPKEQMAKDVS L TCMITDFFPEDITVEWQW NGQPAENYKNTQPIMDTDGSYFVYSKLVNQSWEAGNTFTCSVLHEGLHNHHTKSLSHSPGK GCCAAAACGACACCCCATCTGTCTATCACTGCGCCCTGGATCTGTCTGCCAACTAACTCCAT GGTGACCTGGGATGCTGTGTAAGGGTATTTCCCTGAGCCAGTGACAGTGACCTGGAACCTCTG GATCCCTGTCCAGCGGTGTGCACACCTTCCAGCTGTCTGAGTCTGACCTTACACTCTGAGC AGCTCAGTGACTGTCCCTCCAGCACCTGGCCAGGAGACCGTCACTGCAACGTTGCCACCC GGCCAGCAGCACCAAGGTGGACAAGAAATTTGCCAGGGATTGGTGTGAAGCCTTGCAATAT GTACAGTCCAGAAAGTATCATCTGTCTTCTCTTCCCCCAAGCCCAAGGATGTGCTCACCATT ACTCTGACTCCTAAGGTACGT CAGCTGGTTGTAGATGATGTGGAGGTGCACACAGTCAAGACGCAACCCCGGAGGAGCAGTCA ACAGCACTTCCGCTCAGTCAGTGAACCTCCATCATGCACAGGACTGGCTCAATGGCAAGGAG TTCAATGCAGGGTCAA CAGTGCAGCTTCCCTGCCCATCGAGAAACCATCTCCAAACCAA AGCAGACCGAAGGCTCCAGAGGTACACCATTCACCTCCAAAGGAGAGATGGCCAAAGGATA AAGTCAGTCTGACCTCCATGATAACAGACTTCTTCCCTGAACA CATTACTGTGGACTCCCACTGG AATGGCAGCCAGCGGAGAACTACAAGAACACTCAGCCCATCATGGACACAGATGGCTTACTT CGTCTACAGCAAGCTCAATGTGCAGAGAGCAACTGGGAGGAGGAAATATTTCACCTGCTCTG TGTTACATGAGGGCTGCACAAACCATCTGAGAAAGAGCTCTCCCACTCTCCTGGTAAA GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNK YAASSYLSTPEQWKSHKYSQVTHEGSTVEKTVAPTECS
245.	murine IgG1 heavy chain constant region	murine	aa	GGTCAAGTGGAGCTGTATCATCTCTTCTTGTAGCAACAGCTACAGGTGTACACTCC
246.	murine IgG1 heavy chain constant region	murine	nt	AKTTPPSVYPLAPGSAQNSMVTGLCLVKGYPEPVTVTWNSGSLSSGVHTFPAVLQSDLYTLS SSVTVPSSTWPSSETVTCNVAHPASSTKVDKKIVPRDCGCKPCICTVPEVSSVFIFFPKPKDVLTI TLTPKVTGVVDISKDDPEVQFSWFVDDEVHTAQTPREEQNFSTRVSSELPIMHQDWLNGKE FKCRVNSAAFPAPIEKTISKTKGRPKAPQVYTIIPPKEQMAKDVS L TCMITDFFPEDITVEWQW NGQPAENYKNTQPIMDTDGSYFVYSKLVNQSWEAGNTFTCSVLHEGLHNHHTKSLSHSPGK GCCAAAACGACACCCCATCTGTCTATCACTGCGCCCTGGATCTGTCTGCCAACTAACTCCAT GGTGACCTGGGATGCTGTGTAAGGGTATTTCCCTGAGCCAGTGACAGTGACCTGGAACCTCTG GATCCCTGTCCAGCGGTGTGCACACCTTCCAGCTGTCTGAGTCTGACCTTACACTCTGAGC AGCTCAGTGACTGTCCCTCCAGCACCTGGCCAGGAGACCGTCACTGCAACGTTGCCACCC GGCCAGCAGCACCAAGGTGGACAAGAAATTTGCCAGGGATTGGTGTGAAGCCTTGCAATAT GTACAGTCCAGAAAGTATCATCTGTCTTCTCTTCCCCCAAGCCCAAGGATGTGCTCACCATT ACTCTGACTCCTAAGGTACGT CAGCTGGTTGTAGATGATGTGGAGGTGCACACAGTCAAGACGCAACCCCGGAGGAGCAGTCA ACAGCACTTCCGCTCAGTCAGTGAACCTCCATCATGCACAGGACTGGCTCAATGGCAAGGAG TTCAATGCAGGGTCAA CAGTGCAGCTTCCCTGCCCATCGAGAAACCATCTCCAAACCAA AGCAGACCGAAGGCTCCAGAGGTACACCATTCACCTCCAAAGGAGAGATGGCCAAAGGATA AAGTCAGTCTGACCTCCATGATAACAGACTTCTTCCCTGAACA CATTACTGTGGACTCCCACTGG AATGGCAGCCAGCGGAGAACTACAAGAACACTCAGCCCATCATGGACACAGATGGCTTACTT CGTCTACAGCAAGCTCAATGTGCAGAGAGCAACTGGGAGGAGGAAATATTTCACCTGCTCTG TGTTACATGAGGGCTGCACAAACCATCTGAGAAAGAGCTCTCCCACTCTCCTGGTAAA GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNK YAASSYLSTPEQWKSHKYSQVTHEGSTVEKTVAPTECS
247.	human lambda light chain constant region	human	aa	GGTCAAGTGGAGCTGTATCATCTCTTCTTGTAGCAACAGCTACAGGTGTACACTCC
248.	human lambda light chain constant region	human	nt	AKTTPPSVYPLAPGSAQNSMVTGLCLVKGYPEPVTVTWNSGSLSSGVHTFPAVLQSDLYTLS SSVTVPSSTWPSSETVTCNVAHPASSTKVDKKIVPRDCGCKPCICTVPEVSSVFIFFPKPKDVLTI TLTPKVTGVVDISKDDPEVQFSWFVDDEVHTAQTPREEQNFSTRVSSELPIMHQDWLNGKE FKCRVNSAAFPAPIEKTISKTKGRPKAPQVYTIIPPKEQMAKDVS L TCMITDFFPEDITVEWQW NGQPAENYKNTQPIMDTDGSYFVYSKLVNQSWEAGNTFTCSVLHEGLHNHHTKSLSHSPGK GCCAAAACGACACCCCATCTGTCTATCACTGCGCCCTGGATCTGTCTGCCAACTAACTCCAT GGTGACCTGGGATGCTGTGTAAGGGTATTTCCCTGAGCCAGTGACAGTGACCTGGAACCTCTG GATCCCTGTCCAGCGGTGTGCACACCTTCCAGCTGTCTGAGTCTGACCTTACACTCTGAGC AGCTCAGTGACTGTCCCTCCAGCACCTGGCCAGGAGACCGTCACTGCAACGTTGCCACCC GGCCAGCAGCACCAAGGTGGACAAGAAATTTGCCAGGGATTGGTGTGAAGCCTTGCAATAT GTACAGTCCAGAAAGTATCATCTGTCTTCTCTTCCCCCAAGCCCAAGGATGTGCTCACCATT ACTCTGACTCCTAAGGTACGT CAGCTGGTTGTAGATGATGTGGAGGTGCACACAGTCAAGACGCAACCCCGGAGGAGCAGTCA ACAGCACTTCCGCTCAGTCAGTGAACCTCCATCATGCACAGGACTGGCTCAATGGCAAGGAG TTCAATGCAGGGTCAA CAGTGCAGCTTCCCTGCCCATCGAGAAACCATCTCCAAACCAA AGCAGACCGAAGGCTCCAGAGGTACACCATTCACCTCCAAAGGAGAGATGGCCAAAGGATA AAGTCAGTCTGACCTCCATGATAACAGACTTCTTCCCTGAACA CATTACTGTGGACTCCCACTGG AATGGCAGCCAGCGGAGAACTACAAGAACACTCAGCCCATCATGGACACAGATGGCTTACTT CGTCTACAGCAAGCTCAATGTGCAGAGAGCAACTGGGAGGAGGAAATATTTCACCTGCTCTG TGTTACATGAGGGCTGCACAAACCATCTGAGAAAGAGCTCTCCCACTCTCCTGGTAAA GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNK YAASSYLSTPEQWKSHKYSQVTHEGSTVEKTVAPTECS

249.	c-terminal domain construct of human MCSP	human	aa	
250.	c-terminal domain construct of human MCSP	human	nt	

<p>251.</p>	<p>partial sequence of cynomolgus MCSP</p>	<p>cynomolgus</p>	<p>aa</p>	<p> GTTGATCCAGGACCCAGTATGGGCATCTCTGTGGCGGGCGGCCACCTCGGCCTTCAGCC AATTCAGATAGACAGGCGAGGTGGTCTTTGCTTCAACAACTCCTCCTCCTCATGACCAC TTCAGAGTCTGGCAGTGGCTAGGGGTGTCATGATCAGCGTAGTGAAGTCACTGTGAGGGC TCTGCTGATGTGGCAGGTGGCCATGGCCAGGGTCCACCTGGCCCTGGACCCACCG TCCTAGATGTGGCAGGTGGCCAAACGACACAGACAGTGTCCGCGCTTCGCTCCTGGAGGA CCGCGCATGGCGGTGGTCCGCGTCCCGAGCAGGACGAGCCGGGGGAGCCAGCTGGT GGACAGTTCATCAGCAGGACCTTGGAGCGGAGGTGGGTGGAGTGGCAGGCGCAGAGG GGAGGCCCCGGCCCCGAGGTGACAGTCTACTCTGGAGCTGTGGGACAGGGGTCCGCT GCTGTGGCTCCCTGACTTTGCCACTGAGCCTTAAATGCTGCCGCGCTACAGCTGGCCT GCTCAGTGTCCCGAGGCGCCGACGAGCGGAGGAGGAGCCAGAGCAGCAGCCACAGGCG AGCAGGCCCCCATGCCATCCAGCCTGAGCCGTGTGGCCAGGAGGCTTCCTGAGCTTCTTA GAGCCAAACATGTTACGCTCATCATCCCATGCTGCTGCTTCTCTCTGGCGCTCATCT GCCCTGCTCTTACTCCGAAACGCAACAGCAGGCGGAGCATGACGTCCAGTCCGTGACTG CCAAGCCCCGCAACGGCTGGCTGGTGACACGACAGACTTTCCGAAGTGGAGCCAGGCC ATCCGCTCACAGCTGTGCTGGCCAGGCGGCCCTCCAGGAGGCCAGCTGACCCAGAGCTGT GCAGTCTGCCGACACCAACCTGCCCTTAAATGAGTACTGGTG PSNGRVVLRAPGTEVRSFTQAQIDGGIVLFSHRGTLGGFRFLDGEHTSSGHEFRVTAQKV LLSLEGRSLTVCPSVQPLSSQTLRASSAGTDPQLLLYRVVRGPQLRFLHAQQDSTGEALVN FTQAEVYAGNIIYEHEMPTFEFWEAHDLELQSSPPARDVAATLAVVSFEAACPORESHLWKN KGLWVEGQRAKIMAAALDASNLIASVPSQRLEHDLFQVTFPSRQLLVSEEPHAGQPHFL QSQLAAGQLVYAH:GGGTQDDGFHRAHQFAGATVAGPQTSFAITVRDVNERPPQPAASVP LRI TRGSRAPI SRAQLSVVDPDSAPGEIEYEQRAPHNGFLSLVGGPGFVNRFTQADVDSGRLLA FVANGSSVAGVFLSMSDASPIPLMSLAVDILPSAIEVQLQAPLEVQALGRSSLSQQQLRVVS DREEPTAAYRLIQGPYGHLLVGGQPASATSQLQIDQGEVVFATNFSSSHDHFRLALARGVNA SAVVNTVRALLHVWAGGPWFQATLRDPTILDAGELANRTGSPFRFLLEGPRHGRVVRVPRRA RMEPGGSQVLEQFTQODLEDGRLEVRPEGRAPSPGDSLTLELWAGVPPAVASLDFATEPY NAARPYSVALLSVPEATRTEAGKPESSTPTGEPGPMASSPVPAVAKGGFLGFLEANMFVLIIXC LVLLLLLALIPLIFYLRKRNTGKHVQVLTAKPRNGLAGDTETFRKVEPGQAIPLTAVPGQGP PGQPDPELLOFCRTPNPALKNGQYWV CCCAGCAACGAGCGGTGCTGCGGGCGGGCGGCCACCGAGGTGCGCAGCTTCACGACGGC CCAGCTGGATGGCGGACTCGTGTCTTCTCACAAGAGAACCTGGATGGAGGCTTCGCTTCG GCCTCTCCGATGGCGAGCACACTCTCTGGACACTTCTCCGAGTGACGGCCAGAGCAAGT CTCTCTCGCTGGAGGCGAGCCGACACTGACTGTCTCCAGGGTCCGTGACGCCACTCAGCAG TCAGACCTCAGAGCCAGCTCCAGCGCAGGACAGCAGCCCGAGCTCTCTACCGTGTGGTGC GGGGCCCCAGCTAGCCGGCTGTTCCATGCCAGCAGCAGCAGGAGGAGGCCCTGTGTGAAC TTCACTCAGGACAGGTCTATGCTGGGATATTCTGTATGAGCATGAGATGCCACCCAGGCCCTT CTGGAGGCCCATGATACCCCTAGAGCTCCAGCTGCTCCTCACCACCTGCCCGGACGCTGGTGCCTCA </p>
<p>252.</p>	<p>partial sequence of cynomolgus MCSP</p>	<p>cynomolgus</p>	<p>nt</p>	<p></p>

55					CCCTTGCTGTGGTGTGTCTTTTGGAGCTGCTGTCTCCAGCGCCCCAGCCACCTCTGGAGAAC AAAGGTCTCTGGTCCCCAGGGCCAGGGCCAGATCACCATGGTGCCTGGATGCTCCCAA CCTTTGGCCAGCGTTCCATCATCCAGCGCTAGAGCATGATGTGCTCTCCAGGTACGAGT TCCCAAGCGGGGCCAGCTATTGCTGTCTAGAGACCCCTCCAGCTGGCAGCCCCACTTCTTG CAGTCCAGCTGGTGCAGGGCAGCTAGTGTATGCCACGGCGTGGGGTACCCCAACAGGATGG CTTCACATTTGTCGCCACCTCCAGGGCCAGAGGGGCCACCGTGGCTGGACCCCAACCTCAG AGGCTTTGCCATCACGGTGGGATGTAATAGCGGGCCCCCTCAGCCACAGGCTCTGTCCA CTCGGATCACCCGAGGCTCTCGAGCCCCCATCTCCGGGCCAGCTGAGTGTCTGGAGCCAGA CTCAGTCTCTGGGAGATTGAGTATGAGTCCAGGGCCAGCCCAACAGGCTTCTCAGCCTGG TGGTGGTGGCCCCGGGGCCCGTGAACCGCTTCAGCAAGCCGATGTGGATTGGGGGGCTGGCC TTCGTGGCCAAACGGGAGCAGCTAGCAGGGCTTCCAGCTGAGCATGTCTGATGGGGCCAGCCC ACCGTGCCATGTCCCTGGCGTGGACATCCTACCATCGCCATCGAGTGCAGCTGAGGAC CCTGGAGGTGCCCCAAGCTTTGGGGGCTCCTCACTGAGCCAGCAGCTCCGGGTGTTCA GATAGGAGGAGCCAGAGGAGCATACCGCTCATCCAGGGACCAAGTACGGGCATCTCTGGT GGTGGGCAGCCCGCTCGGCTTCAGCCAACTCCAGATAGACCAGGGCGAGGTGCTTTGCCT TCACCAACTTCTCCTCCTCATGACCATTCAGAGTCTGAGTCTGGCATGGGTAGGGGTGTCAACGA TCAGCCGTAGTGAACATCACTGTGAGGGCTCTGCTGACGTGTGGCAGGTGGGCCATGGCCCCA GGTGCTACCTGCGCTGGACCAACCATCTCTAGATGCTGGCAGTGGCCAAACCGCACAGGCA GTGTCCCCGCTTCGCTCCTGGAGGACCCCGCATCCCGCTGTCCGTCTGCCCGCAGCC AGGATGGAGCTGGGGGAGCCAGCTGGTGGAGCAGTCACTCAGCAGGACCTTGGAGTGGGAG GCTGGGCTGGAGTGGGAGCCAGGAGGAGGAGGCCCCCAGCCCCCAGGGGACAGTCTCACTC TGGAGCTGTGGGCACAGGGCTCCACCTGTGTGGCTCCTCGACTTGGCACTGAGCCTTAC AATGCTGCCCGGCTACAGGTGGCCCTGCTCAGTGTCCCCGAGGCCACCCGGACGGAAGCAGG GAAGCCAGAGAGCAGACCCCCACAGGGAGCCAGGCCCCATGGCATCTAGCCCTGTGCTGTG TGCCCAAGGAGGCTTCTGGGCTTCTTGGAGCCCAACATGTTCACTCATATCCCTGTGTC CTGTCCTTCTGCTCCTGGGCTCATCTTGGCCCTGCTCTTACCTCCGAAACGCAACAGAC GGGCAAGCATGACGTCCAGGTCTGACTGCCAAGCCCGCAATGGTCTGGTGGTGCACATGAGA CCTTCGCAAGGTGGAGCCAGGCCAGGCCATCCGCTCACAGCTGTGCCTGGCCAGGGGCCCT CCGGAGGCCAGCCTGACCCAGAGCTGTGAGTCTGCGCGGACACCCCAACCTGCCCTTAAGAA TGGCAGTACTGGGTG
253.	PCR primer for CD3 ϵ chain - forward primer	artificial	nt		AGACTCTGGGCCTCTGC
254.	PCR primer for CD3 ϵ chain - reverse primer	artificial	nt		CGGATGGGCTCATAGTCTG
255.	His6-human CD3 ϵ	artificial	aa		HHHHHQDGNEMGGITQTPYKVSISGTTVILTQPYPGSEILLQHNNDKNIIGDEDDKNIIGSEDD

256.	His6-human CD3ε	artificial	nt	<p>HLSLKEFSELEQSGYVVCYPRGSKPEDANFYLYLRVCEMCMEMDMVSVATIVIVDICITGGILL LLVYYSKNRKAKAPVTRGAGAGGRQGRQNKERPVPVNPNDYEPKRGQDLYSLNQRRRI ATGGATGGAGCTGTATCATCCTCTCTTGGTAGCAACAGCTACAGGTGTACACTCCCCTCATCA CCATCATCATCAAGATGGTAATGAAGAAATGGGTGGTATACACAGACACCATATAAAGTCTCCA TCTCTGGAACACACAGTAATAATTGACATGCCCTCAGTATCCTGGATCTGARATATATGGAACAC AATGATAAAAACATAGGCGGTGATGAGGATGATAAAAACATAGGAGTGAAGGATCACTGTCTC ACTGAAGGAATTTTCAGAAATGGAGCAAAGTGTATTATGTCTGCTACCCAGAGGAAGCAAAAC CAGAAGATGCGAACTTTTATCTCTACCTGAGGCGACGCTGTGAGAACTGCATGGAGATGGAT GTGATGTCGGTGGCCACAATGTCTATGTGACATCTGCATCACTGGGGCTTGTCTGCTGCTGGT TACTACTGGAGCAAGAAIAGAAAGGCCAAGCCCTGTCTCCCAACCCAGACTATAGAGCCCATC GCAGCAAAAGGGGACAAAACAAGGAGAGGCCACACCTGTTCCTGCTGCTGAGAGCGCATC CGAAAGCCACGCGGACCTGTATTCTGGCTGCTGCTGAGAGCGCATC</p>
257.	CD33 AH3 HL x H2C HL	artificial	aa	<p>QVQLVQSGAEVKKPESVKVSCKASGYFTNYGMNWRVQAPGQGLEWMGWINTYTGEPTVADDFK GRVTMSSDTSTAYLEINSLRSDDTAIYICARWSWDGYVYFDYWQQGTTVTVSS9999s999 9s9999sDIVMTQSPDLSLVSLGERTTINCKSSQVLDSSKNKNSLAWYQQKPGQPPKLLLSWAS TRESGIPDRFSGSGSGTDFTLTIDSLQPEDSATYCYQQSAHFPIITFGQGRLEIKSGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAMNWRVQAPGKLEWVARIRSKYNNYATVYADSVKDR FTISRDDSKNTAYLQMNKLKTEDTAVYCVRHGNFGNSYISYWAYWGQGLTIVTSSGGSGSGGG SGGGSTVVTQEPSTLVSPGGTTLTLCGSTGAVTSGYYPNWVQKPGQAPRGLIGSTKFLAPG TPARFSGSLGGKAALTLSGVQPEDEAEYICALWYSNRWVFGGKLTVL</p>
258.	CD33 AH3 HL x H2C HL	artificial	nt	<p>CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAAGCCCTGGAGAGTCAGTCAAGGTCTCCTG CAAGCTAGCGGGTATACCTTCACAACTATGGAATGAACCTGGTGAGGCGAGGTCCAGGACAGG GTTTAGAGTGATGGCTGGATAAACACCTACACTGGAGAGCCACATATGCTGATGACTTCAAG GGACGGGTTACCATGTCTTCGGATACCTCTACAGCACTGCCTATTTGGAATCAACAGCCTCAG AAGTGATGACACGGCTATATATTACTGTGGCGCTGGAGTGGAGTGTGTTACTACGTTACT TTGACTACTGGGGCCAAAGGCACACTACGGTCACGCTCTCTCAGGTGGTGGTGTCTGGCGCGGC GGCTCCGGTGGTGGTCTTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCT GGCGAGAGGACCACTCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCAGAAATAAGA ACTCCTTAGCTTGGTACCAGAGAAACCAGGACAGCTCCTAAATTACTCCTTTCTGGGCATCT ACGCGGGAATCCGGGATCCCTGACCGATTCACTGGCAGCGGTCTGGGACAGATTTTCACTCTCAC TATTGACAGCTGCAGCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCCACTTCCCGA TCACCTTTGGCCAAAGGACACGACTGGAGATTAAATCCGAGGTGGTGGCTCCGAGGTGCACTG GTCGAGTCTGGAGGAGGATTGGTGCAGCTGGAGGTCAATTGAAACTCTCATGTGCAAGCTCTGG ATTACACCTTCAATAAGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGGGTTTGGAAATGGG TTGCTCGCATAGAAGTAATAATAATAATATGCAACATATATTGCCGATTTCAGTGAAGACAGG TTCACCATCTCCAGAGATGATTCAAAACACTGCCTATCTACAAATGAACAACTTGAACAACTGA GGACACTGCCGTGTACTACTGTGTGAGACATGGGAACCTCGGTAATAGCTACATATCCTACTGGG</p>

				CTTACTGGGGCCAAAGGACTCTGGTCAACCGTCTCCTCAGGTGGTGGTGGTCTGGCGGGCGGGCGGCTCCGGTGGTGGTGGTCTCAGACTGTTGTGACTCAGGAACCTTCACTCAACGTATCAACCTGGTGGAACAGTCACACTCACTGTGGTCTCAGACTGGGCTGTATCATCTGGCTACTACCAAACTGGGTCCAACAAAACAGGTCAAGCACCCCGTGGTCTAATAGGTGGACTAAGTTCCTCGCCCCCGGTACTCCTGCCAGATTCTCAGGCTCCCTGCTTGAGGCAAGGCTGCCCTCAACCTCTCAGGGGTACAGCAGAGGATCAGGCAGAAATATTACTGTGCTCTATGTTACAGCAACCGCTGGGTGTTCGGTGGAGAACCAACTGACTGCTCTA
259.	CD33 AH3 HL x F12Q HL	artificial	aa	QVQLVQSGAEVKKPGESVKVSKASGYFTNYGMNWVRQAPGQGLEWMGWINTYTGEPTVADDFKGRVTMSDSTSTAYLEINSLRSDDTAIYCARWSWSDGYVYFDYWGQGTITVTVSSggsggg9s9999sDIVMTQSPDSLIVSLGERTTINCKSSQSVLDSKNKNSLAWYQQKPGQPPKLLLSWASTRESGIPDRFSGSGSGTDFTLTIDSLQPEDSATYQCQSAHFPIITFGQGRLEIKSGGGSEVQLVESGGGLVQPGGSLKLSCAAAGFTFNSYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSVKGRFTISRDDSKNTAYLQMNNLLKTEDTAVYCYVRHGTFNSYVSWWAYWGQTLVTVSSGGGGSGGGSGGGGQTVVTQEPSTVSPGGTTLTCSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTPARFSGSLGGKAALTLSGVQPEDEAEYCVLWYSNRWVFGGKLTVL
260.	CD33 AH3 HL x F12Q HL	artificial	nt	CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAAAGCCTGGAGAGTCAGTCAAGTCTCCTGCAAGGTAGCGGGTATACCTTCACAACTATGGAATGAAGTGGTGAGGAGGCTCCAGGACAGGGTTTAGAGTGATGGCTGGATAAACACCTACACTGGAGAGCCAAACATATGCTGATGACTTCAAGGGACGGGTACCATGTCTTCGGATACCTTACCAGCACTGCCTATTGGAAATCAACAGCCTCAGAAGTGATGACACGGCTATATATTACTGTGGCGCTGGAGTGGAGTGGTACTACGTTTACTTTGACTACTGGGGCCAAAGGCACACTACGGTCAACGCTCCTCAGGTGGTGGTCTGGCGGGCGGCGGTCCGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTCTCTGGCGAGAGGACCAACCACTCAACTGCAAGTCCAGCCAGAGTGTITTAGACAGTCCCAAGAAATAAGAATCCTTAGCTTGGTACCAGCAGAAACCCAGGACAGCCTCCTAAATTACTCCTTCCCTGGGCATCTACCGGGGAATCCGGGATCCCTGACCGATTCAAGTGGCAGCGGTCTGGGACAGATTCACTCTCACATTGACAGCTGCAGCTGAAGATTCTGCACTTACTATTGTCAACAGTCTGCCACTTCCCGATCACCTTTGGCCAAAGGACACGACTGGAGATTAAATCCGAGGTGGTGGTCCGAGGTGACGCTGTCGAGTCTGGAGGAGGATTGGTGCAGCTGAGGTGAGGTCAITGAACCTCTCATGTGCAGCCTCTGGATTCACTTCAATAGCTACGCCATGAAGTGGTCCGCGAGGCTCCAGGAAAGGTTTGGAAATGGGTTGCTCGCATAGAAGTAATAATAATTATGCAACATATATTGCCGATTTCAGTGAAGGCAGGTTCAACCATCTCCAGAGATGATTCAAAAACACTGCCATCTACAAATGAACAACTTGAACAACTGAGACACTGCCGTGTACTACTGTGTGAGACATGGGAACCTCGGTAAATAGTACGTTTCTGTGGTGGCTTACTAGGGGCAAGGACTCTGGTACCGTCTCCTCAGGTGGTGGTCTGGCGGGCGGGCGGCTTACCTGGTGGTGGTCTCAGACTGTTGTGACTCAGGAACCTTCACTCAACGTATCACTGGTGGAACAGTCACACTGAGTGTGGTCTCAGCTGGGCTGTATCTGGAACACTACCCAACTGGGTTCCAAACAAAACAGGTCAGGACCCCGTGGTCTAATAGTGGGACTAAGTTCCTCGCCCCCGGTACTCCTGCCAGATTCTCAGGCTCCCTGCTTGAGGCAAGGCTGCCCTCAACCTCTCAGGGGTACA

261.	CD33 AH3 HL x 12C HL	artificial	aa	<p>GCCAGAGGATGAGGCAGAAATATTACTGTGTTCTATGTTACAGCAACCGCTGGGTGTTTCGGTGGAG GAACCAAACTGACTGTCTTA</p> <p>QVQLVQSGAEVKKPGESVKVSKASGYFTFTNYGMNWRQAPQGQLEWMGWINTYTGEPTYADDFK GRVTMSDTSSTAYLEINSLRSDDTAIYICARWSWDGYVYFDYWGQGTITVTVSS999s999 9s999sDIVMTQSPDSLTVSLGERTTINCKSSQSLDSSKNKNSLAWYQQKPGQPPKLLLSWAS TRESGIPDRFSGSGSGTDFTLTIIDSLQPEDSATYCCQSAHFPIITFGQGTGLEIKSGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYVADSVKDR FTISRDDSKNTAYLQMNLLKTEDTAVYICVRHGFNSYISYWAYWGQGTITVTVSSGGGSGGGG SGGGSGTQVVTQEPSTVSPGGTVTLTCSSTGAVTSGNYPNWVQQKPGQAPRGLIGITKFLAPG TPARFSGSLGGKAALTLSGVQPEDEAEYICVLWYSNRWVFGGKLLIVL</p> <p>CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAAAAGCCTGGAGAGTCAGTCAAGGTCTCCTG CAAGGCTAGCGGGTATACCTTCACAACTATGGAATGAACTGGTGAGGCAAGCTCCAGCACAGG GTTAGAGTGGATGGCTGGATAAACACCTACACTGGAGAGCCACATATGCTGATGACTTCAAG GGACGGGTACCATGCTTCGGATACCTTACAGCACTGCCTATTGGAAATCAACAGCCTCAG AAGTGATGACACGGCTATATATTACTGTGCGGCTGGAGTTGGAGTATGGTTACTACGTTTACT TTGACTACTGGGGCAAGGCACACTACGGTCACTGATGACACAGTCCAGACTCCCTGACTGTGTCTCT GGTCCGGTGGTGGTCTCTGACATCGTATGACACAGTCCAGACTCCCTGACTGTGTCTCT GGCGAGAGGACCACTCAACTGCAAGTCAGCCAGAGTGTITTAGACAGTCCCAAGAAATAGA ACTCCTTAGCTTGGTACCAGCAGAAACAGGACAGCTCCTAAATTACTCTTCTGGGCATCT ACGGGGAATCCGGATCCCTGACCGATCACTAGTGGCAGCGGTCTGGACAGATTCACTCTCAC TATTGACAGCTGCAGCTGAAGATTCTGCACTTACTATTGTCAACAGTCTGCCACTTCCCGA TCACCTTTGGCCAAAGGACACGACTGGAGATAAATCCGAGGTGTTGGTCCGAGGTGCAGCTG GTCGAGTCTGAGGAGGATTGGTGCAGCTGGAGGTCAATTGAACTCTCATGTGCACTCTGG ATTACCTTCAATAAGTACGCCATGAAGTGGTCCGCCAGGTCCAGGAAAGGTTTGGAAATGGG TTGCTCGCATAAAGTAATAATAATAATATGCAACATATATGCCGATTTCAGTGAAGACAGG TTCACCATCTCCAGAGATGATTCAAAAACACTGCCTATCTACAAATGAACAACTGAAAACTGA GGAACTGCGGTGTACTACTGTGAGACATGGAACTTCGGTAATAGCTACATATCTACTGGG CTTACTGGGGCCAAAGGACTCTGGTACCGTCTCCTCAGGTGGTGGTCTTGGGGGGGGGGC TCCGGTGGTGGTGTCTCAGACTGTGACTCAGGAACCTTCACTCACCGTATACCTGGTGG AACAGTCACACTCACTTGTGGTCTCTGACTGGGCTGTACATCTGGCACTACCCAACTGGG TCCAAACAAAACCAAGTCAGGCACCCCGTGTCTAATAGTGGGACTAAGTCTCTCGCCCCGGT ACTCTGCCAGATTCTCAGGCTCCCTGCTGGAGGCAAGGTGCCCTCACCTCTCAGGGGTACA GCCAGAGGATGAGGCAGAAATATTACTGTGTTATGTTACAGCAACCGCTGGGTGTTTCGGTGGAG GAACCAAACTGACTGTCTTA</p>
262.	CD33 AH3 HL x 12C HL	artificial	nt	<p>CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAAAAGCCTGGAGAGTCAGTCAAGGTCTCCTG CAAGGCTAGCGGGTATACCTTCACAACTATGGAATGAACTGGTGAGGCAAGCTCCAGCACAGG GTTAGAGTGGATGGCTGGATAAACACCTACACTGGAGAGCCACATATGCTGATGACTTCAAG GGACGGGTACCATGCTTCGGATACCTTACAGCACTGCCTATTGGAAATCAACAGCCTCAG AAGTGATGACACGGCTATATATTACTGTGCGGCTGGAGTTGGAGTATGGTTACTACGTTTACT TTGACTACTGGGGCAAGGCACACTACGGTCACTGATGACACAGTCCAGACTCCCTGACTGTGTCTCT GGTCCGGTGGTGGTCTCTGACATCGTATGACACAGTCCAGACTCCCTGACTGTGTCTCT GGCGAGAGGACCACTCAACTGCAAGTCAGCCAGAGTGTITTAGACAGTCCCAAGAAATAGA ACTCCTTAGCTTGGTACCAGCAGAAACAGGACAGCTCCTAAATTACTCTTCTGGGCATCT ACGGGGAATCCGGATCCCTGACCGATCACTAGTGGCAGCGGTCTGGACAGATTCACTCTCAC TATTGACAGCTGCAGCTGAAGATTCTGCACTTACTATTGTCAACAGTCTGCCACTTCCCGA TCACCTTTGGCCAAAGGACACGACTGGAGATAAATCCGAGGTGTTGGTCCGAGGTGCAGCTG GTCGAGTCTGAGGAGGATTGGTGCAGCTGGAGGTCAATTGAACTCTCATGTGCACTCTGG ATTACCTTCAATAAGTACGCCATGAAGTGGTCCGCCAGGTCCAGGAAAGGTTTGGAAATGGG TTGCTCGCATAAAGTAATAATAATAATATGCAACATATATGCCGATTTCAGTGAAGACAGG TTCACCATCTCCAGAGATGATTCAAAAACACTGCCTATCTACAAATGAACAACTGAAAACTGA GGAACTGCGGTGTACTACTGTGAGACATGGAACTTCGGTAATAGCTACATATCTACTGGG CTTACTGGGGCCAAAGGACTCTGGTACCGTCTCCTCAGGTGGTGGTCTTGGGGGGGGGGC TCCGGTGGTGGTGTCTCAGACTGTGACTCAGGAACCTTCACTCACCGTATACCTGGTGG AACAGTCACACTCACTTGTGGTCTCTGACTGGGCTGTACATCTGGCACTACCCAACTGGG TCCAAACAAAACCAAGTCAGGCACCCCGTGTCTAATAGTGGGACTAAGTCTCTCGCCCCGGT ACTCTGCCAGATTCTCAGGCTCCCTGCTGGAGGCAAGGTGCCCTCACCTCTCAGGGGTACA GCCAGAGGATGAGGCAGAAATATTACTGTGTTATGTTACAGCAACCGCTGGGTGTTTCGGTGGAG GAACCAAACTGACTGTCTTA</p>
263.	CD33 AF5 HL x H2C HL	artificial	aa	<p>QVQLVQSGAEVKKPGASVKVSKASGYFTFTNYGMNWRQAPQGQLEWMGWINTYTGEPTYADDFK GRVTMSDTSSTAYLELHNLRSDDTAIYICARWSWDGYVYFDYWGQGTITVTVSS999s999 9s999sDIVMTQSPDSLTVSLGERTTINCKSSQSLDSSKNKNSLAWYQQKPGQPPKLLLSWAS</p>

127

266.	CD33 AF5 HL x F12Q HL	artificial	nt	<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p> <p>35</p> <p>40</p> <p>45</p> <p>50</p> <p>55</p> CAGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAACCTGGAGCGTCAAGTCAAGTCTCTCTG CAAGGCTAGCGGGTATACCTTCACAAACTATGGAATGAAGTGGTGAAGCAGGCTCCAGGACAGG GTTAAAGTGGATGGCTGGATAAACACCTACACTGAGAGCCAAACATATGCTGATGACTTCAAG GGACGGGTACCATGACTTCGGATACCTCTACAGCACTGCCTATTTGGAACCTCCACAACTCAG AAGTATGACACACGGCTGTATATTACTGTGGCTGGAGTTGAGTGAAGTTACTACGTTTACT TTGACTACTGGGCCAAGGCACTACGGTACCGTCTCTCAGGTGGTGGTGGTCTGGCGGGC GGCTCCGGTGGTGGTCTGACATCGTGTGATGACACAGTCTCCAGACTCCCTGACTGTCTCT GGCGAGAGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTAGACAGCTCCAGAAATAAGA ACTCCTTAGCTTGTACCAAGAGAACCCAGGACAGCTCCTAAATTACTCCTTTCTGGGCATCT ACGGGGATCCGGATCCCTGACCGATTCTGCAACTTACTATTGTCAACAGTCTGCCACITCCCGA TATTGACAGCTGCAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACITCCCGA TCACCTTTGGCCAAAGGACACAGCTGGAGATTAAATCCGAGGTGGTGGTCCGAGGTGCAGCTG GTCAGTCTGGAGGAGGATTGGTGACCGCTGGAGGCTCAATGAACTCTCATGTGAGCCTCTGG ATTACCTTCAATAGCTACGCCATGAAGTGGTCCGCCAGGCTCCAGGAAAGGTTTGAATGGG TTGCTCGCATAGAAGTAAATATAATATATGCAACATATATGCCGATTCTGAGTGAAGGACAG TTCACCATCTCCAGAGATGATTCAAAAACACTGCCTATCTACAAATGAACAACTTGAATACTGA GGACACTGCCGTACTACTGTGTGAGACATGGAACTTCGGTAATAGTACGTTCTCTGGTGGG CTTACTGGGGCCAAAGGACTCTGGTCACCGTCTCTCAGTGGTGGTGGTCTGGCGGGCGCGC TCCGCTCCTGCTCTCTCAGACTGTGTGACTCAGCAACCTTCACTCAACGATACACTGCTGG AACAGTCACACTCACTTGTGGTCTCTGACTGGGCTGTACATCTGGCAACTACCAAACTGGG TCCAAACAAACACAGGTCAAGCAACCTGGTCTTAATAGTGGGACTAAGTCTCTGCCCGCGGT ACTCCTGCCAGATTCTCAGGCTCCCTGCTTGAGGCAAGCTGCCCTCACCTCTCAGGGGTACA GCCAGAGGATGAGGCAGATATTACTGTGTCTATGTTACAGCAACCGCTGGGTGTCTCGTGGAG GAACCAAACTGACTGTCTCTA
267.	CD33 AF5 HL x I2C HL	artificial	aa	<p>QVQLVQSGAEVKKPGASVKVCKASGYTFITNYGMNWVKQAPGQGLKWMGWINTYTGEPTIYADDFK GRVTMTSDTSTSTAYLELHNLRSDDTAVYICARWSWSDGYIVYFDYWQGTITVTVSS9999s999 999999sDIVMTQSPDSLTVSLGERTTINCKSSQSVLDSKKNKNSLAWYQQKPGQPKLLSWAS TRESGIPDRFSGSGSGTDFTLTIDSLQPEDSATYICQQSAHFPITFGQGRLEIKSGGGGSEVQL VESGGGLVQPGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYYIADSVKDR FTISRDDSKNTAYLQMNLLKTEDTAVYICVRHGNFNSYISYWAYWGQGLTVTVSSGGGSGSGGG SGGGSGTVVVTQEPSTLVSPGGTITLTCGSSGTGAVTSGNYPNWVQKPGQAPRGLIGSTKFLAPG TPARFSGSLGGKAALTLGVQPEDEAEYICVLWYSNRWVFGGTGKLTVL </p>
268.	CD33 AF5 HL x I2C HL	artificial	nt	<p>CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAACCTGGAGCGTCAAGTCAAGGTCTCTCTG CAAGGCTAGCGGGTATACCTTCACAAACTATGGAATGAAGTGGTGAAGCAGGCTCCAGGACAGG GTTAAAGTGGATGGCTGGATAAACACCTACACTGAGAGCCAAACATATGCTGATGACTTCAAG GGACGGGTACCATGACTTCGGATACCTCTACAGCACTGCCTATTTGGAACCTCCACAACTCAG AAGTATGACACACGGCTGTATATTACTGTGGCTGGAGTTGAGTGAAGTTACTACGTTTACT TTGACTACTGGGCCAAGGCACTACGGTACCGTCTCTCAGGTGGTGGTGGTCTGGCGGGC GGCTCCGGTGGTGGTCTGACATCGTGTGATGACACAGTCTCCAGACTCCCTGACTGTCTCT GGCGAGAGGACCACCATCAACTGCAAGTCCAGCCAGAGTGTAGACAGCTCCAGAAATAAGA ACTCCTTAGCTTGTACCAAGAGAACCCAGGACAGCTCCTAAATTACTCCTTTCTGGGCATCT ACGGGGATCCGGATCCCTGACCGATTCTGCAACTTACTATTGTCAACAGTCTGCCACITCCCGA TATTGACAGCTGCAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACITCCCGA TCACCTTTGGCCAAAGGACACAGCTGGAGATTAAATCCGAGGTGGTGGTCCGAGGTGCAGCTG GTCAGTCTGGAGGAGGATTGGTGACCGCTGGAGGCTCAATGAACTCTCATGTGAGCCTCTGG ATTACCTTCAATAGCTACGCCATGAAGTGGTCCGCCAGGCTCCAGGAAAGGTTTGAATGGG TTGCTCGCATAGAAGTAAATATAATATATGCAACATATATGCCGATTCTGAGTGAAGGACAG TTCACCATCTCCAGAGATGATTCAAAAACACTGCCTATCTACAAATGAACAACTTGAATACTGA GGACACTGCCGTACTACTGTGTGAGACATGGAACTTCGGTAATAGTACGTTCTCTGGTGGG CTTACTGGGGCCAAAGGACTCTGGTCACCGTCTCTCAGTGGTGGTGGTCTGGCGGGCGCGC TCCGCTCCTGCTCTCTCAGACTGTGTGACTCAGCAACCTTCACTCAACGATACACTGCTGG AACAGTCACACTCACTTGTGGTCTCTGACTGGGCTGTACATCTGGCAACTACCAAACTGGG TCCAAACAAACACAGGTCAAGCAACCTGGTCTTAATAGTGGGACTAAGTCTCTGCCCGCGGT ACTCCTGCCAGATTCTCAGGCTCCCTGCTTGAGGCAAGCTGCCCTCACCTCTCAGGGGTACA GCCAGAGGATGAGGCAGATATTACTGTGTCTATGTTACAGCAACCGCTGGGTGTCTCGTGGAG GAACCAAACTGACTGTCTCTA </p>

269.	CD33 AC8 HL x H2C HL	artificial	aa	<p>TTGACTACTGGGCAAGGCACTACGGTCACCGTCTCCTCAGGTGGTGGTCTTGCGCGCGGC</p> <p>GGCTCCGGTGGTGGTCTTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCT</p> <p>GGGCGAGAGGACACCATCAACTGCAAGTCCAGCCAGAGTGTTTAGACAGCTCCAAGAAIAGA</p> <p>ACTCCTTAGCTTGGTACACAGCAAAACAGGACAGCCTCCTAAATTACTCCTTCCCTGGCATCT</p> <p>ACGGGGAATCCGGGATCCCTGACCGATTCACTGGCAGCGGCTGGGACAGATTCACTCTCAC</p> <p>TATTGACAGCCTGCAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCGA</p> <p>TCACCTTTGGCCAAAGGACACGACTGGAGATTAAATCCGGAGGTGGTGGCTCCGAGGTGCAGCTG</p> <p>GTCGAGTCTGGAGGAGGATTGGTGACGCTGGAGGTCATTGAACTCTCATGTGCAGCCTCTGG</p> <p>ATTCACTTCAATAAGTACGCCATGAACCTGGGTCCGCCAGGTCACAGAAAGGTTTGGAAATGGG</p> <p>TTGCTGCATAAGAAATAAATAATAATTAIGCAACATATTATGCCGATTCACTGAAAGACAGG</p> <p>TTCAACCATCCAGAGATGATCAAAAAACACTGCCTCTCAAAATGAACAACTTGAAAACTGA</p> <p>GGACACTGCCGTACTACTGTGTGAGACATGGGAATCTCGGTAACTAGTACATATCCTACTGGG</p> <p>CTTACTGGGCAAGGACTCTGGTCACCGTCTCCTCAGGTGGTGGTGGTCTTGCGCGCGCGGC</p> <p>TCCGGTGGTGGTCTCTCAGACTGTTGTGACTCAGGAACCTTCACTACCGTATCACCTGGTGG</p> <p>AACAGTCACACTCTGTGGCTCCTCGACTGGGCTGTTACATCTGGCAACTACCAAACTGGG</p> <p>TCCAACAAAAACAGGTCAGGCAACCCGTGGTCTAATAGTGGGACTAAGTTCCTCGCCCCGGT</p> <p>ACTCCTGCCAGATTCTCAGGCTCCCTGCTTGGAGGCAAGGTCGCCCTCACCCCTCTCAGGGGTACA</p> <p>GCCAGAGGATGAGCAGAAATATTACTGTGTTCTATGGTACAGCAACCGCTGGGTGTTCCGTGGAG</p> <p>GAACCAAACTGACTGTCTCTA</p> <p>QVQLVQSGAEVKPGESVKVSKASGYFTFTNYGMNWKQAPGQGLKWMGWINTYTGPTYADDFK</p> <p>GRVTMTDTSTSTAYMEIRNLNRDDTAVYYCARWSWSDGYVYFDYWGQGTFTVVS</p> <p>gsgsgsDIIVMTQSPDLSLTSLGERTTINCKSSQVLDSSKNKSLAWYQKPGQPKLLLSWAS</p> <p>TRESGIPDRFSGSGSTDFLTIDSLQPEDSATYYQQSAHFPIFGQGRLEIKSGGSGEVQL</p> <p>VESGGGLVQPGSLKLSAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYYADSVKDR</p> <p>FTISRDDSKNTAYLQMNLIKTEDTAVYYCVRHGNEGNSIYSYWAYWGQGTFTVVS</p> <p>SGGGGSQTVVTQEPSLTVSPGGTTLTCGSSTGAVTSGYYPNWOOPQAPRGLIGGTFKLAPG</p> <p>TPARFSGSLLGKKAALTLSGVQPEDEAEYICALWYSNRWVFGGKTLTVL</p>
270.	CD33 AC8 HL x H2C HL	artificial	nt	<p>CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAGCCCTGAGAGTCAGTCAAGGTCTCCTG</p> <p>CAAGGTAGGGGTATACCTTCACAAACTATGGAATGAACCTGGGTGAAGCAGGCTCCAGGACAGG</p> <p>GTTTAAAGTGGATGGCTGGATAAACACCTACACTGGAGAGCCACATATGCTGATGACTTCAAG</p> <p>GGACGGGTACCATGACTACGGATACCTCTACCAGCACTGCCTATATGAAATCCGCAACCTCAG</p> <p>AAATGATGACACGGCTGTATATTACTGTGCGCTGGAGTTGGAGTGTGTTACTACGTTTACT</p> <p>TTGACTACTGGGCAAGGCACTACGGTCAACCGTCTCCTCAGGTGGTGGTGGTCTTGCGCGCGGC</p> <p>GGCTCCGGTGGTGGTCTGACATCGTGTGATGACACAGTCTCCAGACTCCCTGCTGTCTCT</p> <p>GGGCGAGGACCAACCATCAACTGCAAGTCCAGCCAGAGTGTTTAGACAGCTCCAAGAAATAAGA</p> <p>ACTCCTTAGCTTGGTACACAGCAAAACAGGACAGCCTCCTAAATTACTCCTTTCCCTGGCATCT</p> <p>ACGGGGAAATCCGGATCCCTGACCGATTTCAGTGGCAGCGGCTCGGACAGATTTCACTCTCAC</p>

271.	CD33 AC8 HL x F12Q HL	artificial	aa	<p> TATTGACAGCCTGACGCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCGA TCACCTTTGGCAAGGACACGACTGGAGATTAAATCCGAGGTGGTGGCTCCGAGGTGCAGCTG GTCGAGTCTGAGGAGGATTGGTGACGCTGAGGCTCATTTGAAACTCTCATGTGCAGCCTCTGG ATTCACTTCAATAAGTACCCATGAACCTGGTCCGACGCTCCAGGAAGGTTTGAATGGG TTGCTCGCATAAAGAGTAAATATAATAATATGCAACATATTATGCCGATTCACTGAAAGACAGG TTCACCATCTCCAGAGATGATTCAAAAAACACTGCCTATCTACAAATGAACAACTTGAAAACTGA GGACACTGCCGTGTACTACTGTGTGAGACATGGAACTTCGGTAATAGCTACATATCTCTACTGGG CTTACTGGGCCAAGGACTCTGGTCACCGTCTCTCAGGTGGTGGTGGTGGTGGTGGTGGTGGGCGG TCCGTTGG AACAGTCACACTCATCTGTGGCTCTCGACTGGGCTGTACATCTGGCTACTACCCAACTGGG TCCAAACAAAAACAGGTGAGGACCCCGTGGTCTAATAGTGGGACTAAGTTCCTCGCCCCCGGT ACTCCTGCCAGATTCTCAGGCTCCCTGCTTGAGGCAAGGTCGCCCTCACCCTCTCAGGGGTACA GCCAGAGGATGAGGCAGATAATTACTGTGCTCTATGCTATGCTACAGCAACCGCTGGGTGTTCCGTGGAG GAACCAACTGACTGTCCTA </p>
272.	CD33 AC8 HL x F12Q HL	artificial	nt	<p> QVQLVQSGAEVKKPGESVKVSKASGYFTNYGNMWVKQAPGQGLKWMWINTYTGEPTYADDFK GRVTMTDTSTSTAYMEIRNLNDDTAVYCARWSWDGYVYFDYWGQGTVTTVSSgggsggg gs9gggsDIVMTQSPDSLTVSLGERTTINCKSSQSLDSSKNKNSLAWYQKPKQLLLSWAS TRESGIPDRFSGSGSGTDFTLTIDSLQPEDSATYYCQSAHFPITFGQGTGLEIKSGGGGSEVQL VESGGGLVQPGSLKLSCAASGFTFNSYAMNWVRQAPKGLEWVARIRSKYNNYATYYADSVKGR FTISRDDSKNTAYLQMNLLKEDTAVYYCVRHGFNSYVSWWAYWGQGLTVTVSSGGGGSGGGG SGGGGQTVVTVTQEPSLTVSPGGTVTLTCGSSTCAVTSNYPNWVQKPKGPAPRGLIGGTKFLAPG TPARFSGSLGGKAALTLGSLVQPEDEAEYYCVLWYSNRWVFGGGLTLVL </p>

<p>273.</p>	<p>CD33 AC8 HL x 12C HL</p>	<p>artificial</p>	<p>aa</p>	<p>TTCAACATCTCCAGAGATGATTCAAAAACACAGTGCCTATCTACAAATGAACAACTTGAAACTGA GGACACTGCCGTGTAATACTGTGTGAGACATGGAACTTCGGTAATAGCTACGTTCTCGTGGG CTTACTGGGGCCAAAGGACTCTGGTCACCGTCTCTCAGGTGGTGGTGGTGGTGGTGGTGGG TCCGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGG AACAGTCACACTCACTTGTGGCTCTCGACTGGCTGGTGGTGGTGGTGGTGGTGGTGGTGGTGG TCCAAACAAAAACAGGTGAGGACCCCGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGT ACTCCTGCCAGATTCTCAGGCTCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGCTTACA GCCAGAGGATGAGGCAGAAATATTACTGTGTCTAATGTTACAGCAACCGCTGGTGGTGGTGGG GAACCAAACTGACTGTCTCTA</p>
<p>274.</p>	<p>CD33 AC8 HL x 12C HL</p>	<p>artificial</p>	<p>nt</p>	<p>QVQLVQSGAEVKKPGESVKVSKASGYTFTNVMNWVKQAPGQGLKWMGWINTYTGEPYADDFK GRVTMTTDTSTSTAYMEIRNLNRDDTAVYCARWSWSDYVYFDYWGQGTITVTVSSg99s999 g999s999sDIVMTQSPDSLTVSLGERTTINCKSSQSVLDSSKNKSLAWYQQKPKPPLKLLSWAS TRESGIPDRFSGSGSGTDFTLTIIDSLQPEDSATYCCQSAHFPITFGQGTREIKSGGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAMNVPQAPGKLEWVARIRSKYNNYATYYADSVKDR FTISRDDSKNTAYLQMNLIKTEDTAVYCYVRHGFNYSYISWAYWGQGTITVTVSSGGGSGSGGGG SGGGGQTVVTQEPSTLVSPGGTITLTGSSSTGAVTSGNYPNWPQKPGQAPRGLIGSTKFLAPG TPARFSGSLGGKAAITLSGVOPEDEAEYICVLWYSNRWVFGGTGKLTIVL</p>

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	F12Q HL			<p>GRVTMTSDTSTSTAYMEISSLRSDDTAVYYCARWSWDGYVYFDYWGQGTTVTVSSG999s999 9s9999sDIVMTQSPDSLTVSLGERTTINCKSSQSVLDSSKNKNSLAWYQQKPGPPKLLLSWAS TRESGIPDRFSGSGSGTDFTLTIDSLQPEDSATYCYQQSAHFPIITFGQGTGLEIKSGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNSYAMNVRQAPGKGLEWVARIRSKYNNYATYVADSVKGR FTISRDDSKNTAYLQMNLIKTEDTAVYCYVRHGFNSYVSWAYWGQGTTLTVSSGGGSGGGG SGGGGQTVVTQEPSTVSPGGTVTLTCSSTCAVTSIGNYPNWWQKPGQAPRGLIGTKFLAPG TPARFSGSLIGGKAALTLSGVQPEDEAEYCVLWYSNRVFGGKLTIVL</p>
278.	CD33 AH11 HL x F12Q HL	artificial	nt	<p>CAGGTGCAGCTGGTGCAGCTCGAGTGAAGACCTGGAGAGTCAGTCAAGGTCTCCTG CAAGGCTAGCGGGTATACCTTCACAAACTATGGAATGAAGTGGTGAAGCAGGCTCCAGCACAGG GTTTAAAGTGGATGGCTGGATAAACACCTACACTGGAGAGCCACATATGCTGATGACTTCAAG GGACGGGTTACCATGACTTCGGATACCTTACAGCACTGCCTATATGGAATCAGCAGCCTCAG AAGTGATGACACGGCTGTATATTACTGTGGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACT TTGACTACTGGGGCCAAAGGCACACGGTCACTGCTCCTCAGGTGGTGGTGGTGGTGGTGGTGGT GGCTCCGGTGGTGGTCTGACATCGTGATGACACAGTCCAGACTCCCTGACTGTGTCTCT GGCGAGAGGACCACTCAACTCAAGTCAGCCAGAGTGTTTAGACAGTCCAGAAATAAGA ACTCCTTAGCTTGGTACCAGCAGAAACAGGACAGCTCCTAAATTACTCCTTCCCTGGGCATCT ACGGGGAATCCGGGATCCCTGACCGATTCACTGAGCGGGTCTGGACAGATTCACTCTCNC TATTGACAGCTGCAGCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCGA TCACCTTTGGCCAAAGGACACGACTGGAGATTAAATCCGAGGTGGTGGTCCGAGGTGACGCTG GTCAGTCTGGAGGAGGATTGGTGCAGCTGAGGAGGTCATTGAACTCTCATGTGACGCTCTGG ATTACCTTCAATAGTACGCCATGAAGTGGTCCGCCAGGCTCCAGGAAAGGTTTGAATGGG TTGCTCGCATAGAAGTAAATAATAATAATGCAACATATTATGCCGATTTCAGTGAAGGCAGG TTCACCATCTCCAGAGATGATTCAAAAACACTGCCTATCTACAAATGAACAACCTGAAAACTGA GGACACTGCCGTGTAATACTGTGTGAGACATGGAACTTCGGTAATAGCTACGTTTCTCGTGGG CTTACTGGGGCCAAAGGACTCTGGTACCGTCTCCTCAGGTGGTGGTGGTGGTGGTGGTGGGCG TCCGTGGTGGTGGTCTCAGACTGTGTGACTCAGGAACCTTCACTACCGTATCACTGGTGG AACAGTCACACTCACTTGTGGTCTCTGACTGGGCTGTACATCTGGCACTACCCAAACTGGG TCCAAACAAAACAGGTGAGGACCCCGTGGTCTAATAGTGGGACTAAGTTCCTCGCCCCGGT ACTCCTGCCAGATTCTCAGGCTCCCTGCTTGGAGGCAAGGTCGCCCTCACCTCTCAGGGGTACA GCCAGAGGATGAGGCAGAAATATTACTGTGTCTATGTTACAGCAACCGCTGGGTGTTCGGTGGAG GAACCAAACTGACTGTCTTA</p>
279.	CD33 AH11 HL x I2C HL	artificial	aa	<p>QVQLVQSGAEVKKPGESVKVSCKASGYTFNYGMNWKVQAPCGQLKWMGWINTYTGEPTVADDFK GRVTMTSDTSTSTAYMEISSLRSDDTAVYYCARWSWDGYVYFDYWGQGTTVTVSSG999s999 9s9999sDIVMTQSPDSLTVSLGERTTINCKSSQSVLDSSKNKNSLAWYQQKPGPPKLLLSWAS TRESGIPDRFSGSGSGTDFTLTIDSLQPEDSATYCYQQSAHFPIITFGQGTGLEIKSGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNSYAMNVRQAPGKGLEWVARIRSKYNNYATYVADSVKDR FTISRDDSKNTAYLQMNLIKTEDTAVYCYVRHGFNSYISWAYWGQGTTLTVSSGGGSGGGG</p>

				<p>GGACGGTTACCTTCACTTCGGATACTCTACACAGCACTGCCTATATGGAACTCCGCAACCTCAA AAGTGATGACACGGCTGTATATTACTGTGGCGCTGGAGTTGGAGTGATGGTTACTACGTTTACT TTGACTACTGGGGCCAAGGCACIACGGTCAACGCTCCTCAGGTGGTGGTTCCTGGCGGGCGGC GGCTCCGGTGGTGGTTCGTGACATCGTGAATGACACAGTCTCCAGACTCCATGACTGTGTCTCT GGCGAGAGACCACTCAACTGCAAGTCCAGCCAGAGTGTCTTAGACAGTCCACGAATAAGA ACTCTTAGCTTGGTACCAGCAGAAACCAGGACAGCTCCTAAATTACTCCTTTCCTGGGCATCT ACGGGGGAATCCGGGATCCCTGACCGATTCACTGGCAGCGGTCTGGACAGATTCACTACTCTCAC TATTGACAGCTGCAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCGA TCACCTTTGCCAAGGACACGACTGGACATTAATCCGAGGTGGTGGTCCGAGGTGCAGCTG GTCAGTCTGGAGGAGGATTGGTGACGCTTGAGGGTCAATTGAACTCTCATGTGCAGCCTCTGG ATTACCTTCAATAAGTACGCCATGAACCTGGTCCGCCAGGTCCAGGAAGGTTTGGAAATGGG TTGCTCGCATAAAGAAGTAAATATAATAATATGCAACATATTATGCCGATTCACTGAAAGACAGG TTCACCATCTCCAGAGATGATTCAAAAACACTGCCTATCTACAAATGAACAACCTTGAAACTGA GGACACTGCCGTGTACTACTGTGAGACATGGAACTTCGGTAAATAGTACATATCCTACTGGG CTTACTGGGGCCAAGGACTCTGGTCAACCTCTCCTCAGGTGGTGGTGGTCTGGCGGGCGCGGC TCCGGTGGTGGTGTCTCAGACTGTGTGACTCAGGAACCTTCACTCAACGTATCACTGGTGG AACAGTCACACTCACTTGTGGTCTCTCAGCTGGGCTGTACATCTGGCTACTACCCAAACTGGG TCCAAACAAAACCAGGTGAGGACCCCGTGGTCTAATAGTGGGACTAAGTCTCTGCCCCCGGT ACTCTGCCAGATTCTCAGCTCCCTGCTTCCACCAAGCTGCCCTCACCTCTCAOCCGTACACA GCCAGAGGATGAGGCAGAAATATTACTGTGCTCTATGTTACAGCAACCCGCTGGGTGGTTCGGTGGAG GAACCAACTGACTGTCTTA</p>	283.	CD33 B3 HL x F12Q HL	artificial	aa	<p>QVQLVQSGAEVKKPGESVKVSKASGYFTTNYGMNWVKQAPGQGLEWMGWINTYTGETNYADKFKQ GRVFTSDTSTSTAYMELRNKSDDTAVYCARWSWDGYVYFDYWGQGTITVTVSS999sg99 sg999gsDIVMTQSPDSMTVSLGERTTINCKSSQSVLDSSTNKNLAWYQQKPGQPPKLLLSWAS TRESGIPDRFSGSGSDTFTLTIDSLQPEDSATYQCQSAHFPITFGQGTRLDIKSGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNSYAMNWVRQAPGKLEWVARIRSKYNNYATYYADSVKGR FTISRDDSKNTAYLQMNILKTEDTAVYCVRHGNFGNSYVSWWAYWGQGTITVTVSSGGGGSGGGG SGGGGQTVVTQEPSLTVSPGGTVTLTCGSSITGAVTSGNYPNWVQKPGQAPRGLIGGTKFLAPG TPARFSGSLGGKAALTLSGVQPEDEAEYCYVLWYSNRWVFGGTKLTVL</p>
				<p>CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGACCTCGAGAGTCAGTCAAGGTCTCCTCTG CAAGGCTAGCGGTATACCTTCACAAACTATGAATGAACCTGGTGAAGCAGGCTCCAGGACAGG GTTTAGAGTGGATGGGCTGGATAAACACCTACCTGAGAGACAAACTATGCTCATAGTTCACG GACGCGTTACCTTCAGTTCGGATACTCTACAGCACTCATATGGAACCTCGCAACCTCAA AAGTGATGACACGGCTGTATATTACTGTGCGCGCTGGAGTGGAGTGATGGTTACTACGTTTACT TTGACTACTGGGGCCAAGGCACIACGGTCAACGCTCCTCAGGTGGTGGTTCCTGGCGGGCGGC GGCTCCGGTGGTGGTTCGTGACATCGTGAATGACACAGTCTCCAGACTCCATGACTGTGTCTCT GGCGAGAGGACCACTCAACTGCAAGTCCAGCCAGAGTGTCTTAGACAGTCCACGAATAAGA</p>	284.	CD33 B3 HL x F12Q HL	artificial	nt	

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<p>289.</p>	<p>CD33 F2 HL x F12Q HL</p>	<p>artificial</p>	<p>aa</p>	<p>TCCGGTGGTGGTGGTCTCTCAGACTGTTGTGACTCAGGAACCTTCACTCACCGTATCACCTGGTGG AACAGTCACACTCACTTGTGGCTCCTCGACTGGGCTGTATACATCTGGCTACTACCCAACTGGG TCCAACAAAAAACAGGTAGGACCCCGTGGTCTAATAGGTGGACTAAGTTCCTCGCCCCGGT ACTCCTGCCAGATTCTCAGGCTCCCTGCTGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACA GCCAGAGGATGAGGCAGAAATATTACTGTGCTCTATGGTACAGCAACCGCTGGGTGTTCGGTGGAG GAACCAAACTGACTGTCTTA</p>
<p>289.</p>	<p>CD33 F2 HL x F12Q HL</p>	<p>artificial</p>	<p>aa</p>	<p>QVQLVQSGAEVKKPESVKVSCKASGYFTNYGMNWKQAPGQGLEWMGWINTYTGETNYADKFFQ GRVFTSDTSTSTAYMELRNKSDDTAVYICARWSWDGYVYFDYWGQGTFTVIVSSG999s999 9s999gsDIVMTQSPDLSVSLGERTTINCKSSQSVLDSSTKNLSLAWYQQKPGQPPKLLLSWAS TRESGIPDRFSGSGSGTDFTLTIDSLQPEDSATYCCQSAHFPITFGQGTGLEIKSGGGGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNSYAMNWRQAPGKLEWVARIRSKYNNYATYADSVKGR FTISRDSKNTAYLQMNLLKTEDTAVYICVRHGFNSYVSWWAYWGQGTFTVIVSSGGGSGGGG SGGGGQTVVTQEPSTVSPGGTFTLTGSSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKLAPG TPARFSGSLGGKAALTLSGVQPEDEAEYICVLWYSNRWVFGGKTLTVL</p>
<p>290.</p>	<p>CD33 F2 HL x F12Q HL</p>	<p>artificial</p>	<p>nt</p>	<p>CAGGTGCAGCTGGTGCAGCTCTGGAGCTGAGTGAAGACCTGGAGAGTCAGTCAGGTCTCTCTG CAAGGTAGCGGTATACCTTCACAACTATGGAATGAACCTGGTGAGCAGGCTCCAGGACAGG GTTAGAGTGGATGGCTGGATAAACACCTACACTGGAGAGACAACTATGCTGATAAGTTCAG GGACGCTTACCTTCAGTACCTACCTACAGCACTGCCTATATGAACTCCGCAACCTCAA AAGTGATGACACGGCTGTATATTACTGTGCGCTGGAGTTGGAGTATGTTACTACGTTTACT TTGACTACTGGGCGCAAGGCACTACGCTACCGTCTCCTCAGTGGTGGTGTCTGCGCGCGG GGTCCGGTGGTGGTCTGACATCGTGTGACACAGTCCAGACTCCCTGTCTGTCTCT GGCGAGAGGACCACTCAACTGCAAGTCCAGCCAGAGTGTTTAGACAGCTCCACCAATAAGA ACTCCTTAGCTTGGTACCAGCAGAAACCCAGCAGCCTCCTAAATTACTCCTTTCCTGGGCATCT ACGCGGAATCCGGGATCCCTGACCGATTCACTGCGAGCGGGTCTGGGACAGATTTCACCTCAC TATTGACAGCTGCAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCGA TCACCTTTGGCCAAGGACACGACTGGAGATTAAATCCGAGGTGGTGGCTCCGAGGTGAGCTG GTCGAGTCTGGAGGAGGATTGGTGACGCTGGAGGGTCAATGAACTCTCATGTGACGCTCTGG ATTACCTTCAATAGCTACGCCATGAAGTGGTCCGCCAGGCTCCAGGAAGGGTTTGGAAATGGG TTGCTCGCATAGAAGTAATATAATATTATGCAACATATATGCCGATTCACTGAGAAAGCAGG TTCACCATCTCCAGAGATGATTCAAAAACACTGCCTATCTACAAATGACAACTTGAATACTGA GGACACTGCCGTGACTACTGTGTGAGACATGGGAACTTCGTAATAGTACGTTTCCCTGGTGG CTTACTGGGGCCCAAGGACTCTGGTCACCGTCTCCTCAGTGGTGGTGTCTGGCGGCGGCGC TCCGGTGGTGGTGGTCTCTCAGACTGTTGTGACTCAGGAACCTTCACTCACCGTATCACCTGGTGG AACAGTCACACTCACTTGTGGTCTCTCGACTGGGCTGTATCATCTGGCAACTACCCAACTGGG TCCAACAAAAAACAGGTAGGCAACCCCGTGGTCTAATAGGTGGGACTAAGTTCCTCGCCCCGGT ACTCCTGCCAGATTCTCAGGCTCCCTGCTTGGAGCAAGGCTGCCCTCACCTCTCAGGGGTACA GCCAGAGGATGAGGCAGAAATATTACTGTGTTCTATGGTACAGCAACCGCTGGGTGTTCGGTGGAG</p>

291.	CD33 F2 HL x l2C HL	artificial	aa	<p>GAACCAAACTGACTGTCCTA</p> <p>QVQLVQSGAEVKKPGESVKVCKASGYFTFTNYGMNWKVQAPQGQLEWMGWINTYTGETNYADKFKQ</p> <p>GRVTFTSDTSTSTAYMELRNKLSODTAVYICARWSWSDGYVYFDYWGQGITVTVSSG999sg99</p> <p>9sg999sDIVMTQSPDLSVSLGERTTINCKSSQSVLDSSNKNLSAWYQQKPGQPPKLLISWAS</p> <p>TRESGIPDRFSGSGSGTDFTLTIDSLQPEDSATYCCQSAHFPITFGQGTREIKSGGGGSEVQL</p> <p>VESSGGLVQPGGSLKLSCAASGFTFNKYAMNWKVQAPGKGLEWVARIRSKYNNYATYADSVKDR</p> <p>FTISRDDSKNTAYLQMNKLKTEDTAVYICVRHGFNYSYISWAYWGQGLTIVTSSGGSGSGGGG</p> <p>SGGGSGTQVVTQEPSTVSPGGTTLICGSSGCAVTSIGNYPNWKVQKPGQAPRGLIGTKFLAPG</p> <p>TPARFSGSLGGKAAITLSGVQPEDEAEYICVLWYSNRWVFGGTKLTVL</p>
292.	CD33 F2 HL x l2C HL	artificial	nt	<p>CAGGTGAGCTGGTGCAGTCTGGAGCTGAGTCAAGAACCTGGAGAGTCAGTCAAGGTCTCCTG</p> <p>CAAGGTAGCGGGTATACCTTCACAACTATGGAATGAACCTGGTGAAGCAGGCTCCAGACAGG</p> <p>GTTAGAGTGGATGGCTGGATAAACACCTACACTGGAGAGACAACTATGCTGATAAGTTCAG</p> <p>GGACCGGTTACCTTCACTTCGGATACCTTACCAGCACTGCTATATGGAACCTCCGCAACCTCAA</p> <p>AAGTGATGACACGGCTGATATTAATCTGTGGCGCTGGAGTGGAGTGGTGTCTGCGCGCGGC</p> <p>TTGACTACTGGGCGCAAGGCACACTACGCTACCGCTCTCCTCAGGTGGTGGTGTCTGCGCGCGGC</p> <p>GGCTCCGGTGGTGGTTCIGACATCGTGATGACACAGTCTCCAGACTCCCTGTCTGTCTCT</p> <p>GGCGAGAGGACCAACATCAACTGCAAGTCCAGCCAGAGTGTCTTAGACAGCTCCACGAATAAGA</p> <p>ACTCCTTAGCTTGGTACCAGAGAACCCAGGACAGCTCTCTAAATTAATCTCTTCTGGCATCT</p> <p>ACCGGGAATCCGGGATCCCTGACCGATTACAGTGGCAGCGGTCTGGGACAGATTCACTCTCAC</p> <p>TATTGACAGCTGCAGCTGAAGATTCTGCACTTACTATTGTCAACAGTCTGCCACTTCCCGA</p> <p>TCACCTTTGGCCAAAGGACACGACTGGAGTTAAATCCGAGGTGGTGGTCCGAGGTGAGCTG</p> <p>GTCAGTCTGGAGGAGGATTGGTGCAGCTGGAGGTGATGAACTCTCATGTGCAGGCTCTGG</p> <p>ATTCACCTTCAATAAGTACGCCATGAATGGTCCGCCAGGCTCCAGGAAAGGTTTGGAAATGGG</p> <p>TTGCTCGCATAAAGAGTAAATATAATAATTAAGCAACATATATGCCGATTCAAGTGAAGACAGG</p> <p>TTCAACATCTCCAGAGATGATTCAAAAACACTGCTATCTACAAATGAACAACTTGAAACTGA</p> <p>GGACACTGCCGTGACTACTGTGTGAGACATGGAACTTGGTAATAGCTACATATCTACTGGG</p> <p>CTTACTGGGCGCAAGGACTCTGGTCAACCTCTCTCAGGTGGTGGTGGTGGTGGTGGTGGTGGG</p> <p>TCCGGTGGTGGTGGTCTCAGACTGTGTGACTCAGGAACCTTCACTACCGTATCACCTGGTGG</p> <p>AACAGTCACACTCACTTGTGGCTCTCGACTGGGCTGTACATCTGGCACTACCCAACTGGG</p> <p>TCCACAAAAAACAGGTCAGGCACCCCGTGGTCTAATAGGTGGGACTAAGTTCCTCGCCCGCGT</p> <p>ACTCCTGCCAGATTCTCAGGCTCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACA</p> <p>GCCAGAGGATGAGGCAGATATTAATCTGTGTCTATGTTACAGCAACCGCTGGGTCTCGGTGGAG</p> <p>GAACCAAACTGACTGTCCTA</p>
293.	CD33 B10 HL x H2C HL	artificial	aa	<p>QVQLVQSGAEVKKPGESVKVCKASGYFTFTNYGMNWKVQAPQGQLEWMGWINTYTGETNYADKFKQ</p> <p>GRVTMTDTSTSTAYMEIRNLRSDDTAVYICARWSWSDGYVYFDYWGQGITVTVSSG999sg99</p> <p>9sg999sDIVMTQSPDLSVSLGERTTINCKSSQSVLDSSNKNLSAWYQQKPGQPPKLLISWAS</p> <p>TRESGIPDRFSGSGSGTDFTLTIDGLQPEDSATYCCQSAHFPITFGQGTREIKSGGGGSEVQL</p>

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	F12Q HL			<p>CAAGGCTAGCGGTATACCTTCACAAACTATGGAATGAACCTGGTGAAGCAGGCTCCAGGACAGG GTTTAGAGTGGATGGCTGGATAAACACCTACACTGGAGAGCCAACTATGCTGATAAGTCCAG GGACGCGTTACCATGACTACGATACCTCTACAGCACTGCCTATATGAAATCCGCAACCTCAG AAGTGATGACACGGCTGTATATTACTGTGGGCTGGAGTTGGAGTATGGTTACTACGTTACT TTGACTACTGGGGCAAGCACTACGGTCACTCCCTCCTCAGGTGGTGGTCTTGGCGCGGC GGCTCCGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCT GGGCGAGAGACCACTCAACTGCAAGTCCAGCCAGAGTGTCTTAGACAGCTCCACAATAAGA ACTCCTTAGCTTGGTACCAGCAGAAACAGGACAGCTCCTAAATTAATTAATTAATTAATTA ACGGGGAAATCCGGGATCCCTGACCGATTCACTGGCAGCGGTTCTGGACAGATTCTACTCTC TATTGACGGCTGCAGCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCGA TCACCTTTGGCCAAGGACACGACTGGAGATTAAATCCGAGGTGGTGGCTCCGAGTGCAGCTG GTCAGTCTGGAGGAGGATTGGTGCAGCTGGAGGCTGAACTCTCATGTGCAAGCTCTGG ATTACCTTCAATAGCTACGCCATGAAGTGGTCCGCCAGGCTCCAGGAAAGGTTTGGAAATGGG TTGCTGCATAAGAAGTAAATTAATTAATTAATTAATTAATTAATTAATTAATTAATTAATTA TTCACCATCTCCAGAGATGATTCAAAAACACTGCCATCTACAAATGAACAACTTGAACAACTGA GGACACTGCCGTGTTACTACTGTGTGAGACATGGAACTTGGTAATAGCTACGTTCTCGTGGG CTTACTGGGGCCAAGGACTCTGGTCACCTCTCTCAGGTGGTGGTGGTCTGGCGCGCGGC TCCGTGGTGGTGGTCTCAGACTGTGTGACTCAGGAACCTTCACTCACCGTATCACTGGTGG AACACTCACACTCACTTGTGCTCTCGACTCGGCTCTTACATCTGGCAACTACCCAACTGGG TCCAAACAAAACAGGTGAGGCAACCCGTTGTTCTAAATAGTGGGACTAAGTTCCTCGCCCCGGT ACTCCTGCCAGATTCTCAGGCTCCCTGTTGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACA GCCAGAGGATGAGGCAGAAATTAATTAATTAATTAATTAATTAATTAATTAATTAATTAATTA GAACCAAACTGACTGTCCTA</p>
297.	CD33 B10 HL x l2C HL	artificial	aa	<p>QVQLVQSGAEVKKPGESVKVSKASGYFTFTNYGMNWKQAPQGQLEWMGWINTYTGEPYADKFQ GRVTMTTDTSTSTAYMEIRNLRDDTAVYICARWSWDGYVYFDYWGQGTVTVSSG999sg9g 9s9999sDIVMTQSPDLSLTSLGERTTINCKSSQSVLDSSNNKNSLAWYQKPGQPPKLLLSWAS TRESGIPDRFSGSGSTDFTLTIIDGLQPEDSATYICQQAHPFITFGQGRLEIKSGGGGSEVQL VESGGGIIVQPGSILKISCAASGFTFNKYAMNWRQA PGKGLEWVARIRSKYNNYATYYADSVKDR FTISRDDSKNTAYLQMNLIKTEDTAVYICVRHGFNSYISYWAYWGQGTTLTVSSGGGSGGGG SGGGGQTVVTQEPSTLTVSPGGTTLTLCGSSGTGAVTSNYPNWKQKPGQAPRGLIGGTFKFLAPG TPARFSGSLIGGKAALTLSGVQPEDEAEYCYLWYSNRWVFGGTKLTVL</p>
298.	CD33 B10 HL x l2C HL	artificial	nt	<p>CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGTCAAGCAAGCAAGCTGGTGCAGTCAAGGTCTCCTG CAAGGTAGCGGGTATACCTTCACAAACTATGGAATGAACCTGGTGAAGCAGGCTCCAGACAGG GTTTAGAGTGGATGGCTGGATAAACACCTACACTGGAGAGCCAACTATGCTGATAAGTCCAG GGACGCGTTACCATGACTACGGATACCTCTACAGCACTGCCTATATGAAATCCGCAACCTCAG AAGTGATGACACGGCTGTATATTACTGTGGGCTGGAGTTGGAGTATGGTTACTACGTTTACT TTGACTACTGGGGCAAGGCACTACGGTCAACCTCTCCTCAGGTGGTGGTGGTCTTGGCGCGGC</p>

			<p>GGCTCCGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTCTCT GGGCGAGAGGACACCATCAACTGCAAGTCAGCCAGAGTGTCTTAGACAGCTCCCAATAAGA ACTCTTAGCTTGGTACAGCAGAAACAGGACAGCCTCTTAATTACTCTTCTGGGCATCT ACGCGGAATCCGGATCCCTGACCGATTCACTGGCAGCGTCTGGACAGATTCACTCTCAC TATTGACGGCTGCAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCACTTCCCGA TCACCTTTGGCCAAAGGACACGACTGGAGATAAATCCGGAGGTGGTCCGAGGTGACAGT GTCGAGTCTGGAGGAGATTGGTGCAGCTGGAGGTCAATTGAACCTCTCATGTGACCTCTGG ATTACCTTCAATAAGTACGCCATGAAGTGGTCCGCCAGGTCCAGGAAGGGTTTGGAAATGGG TTGCTGCGATAAGAAGTAAATATAATAATTATGCAACATATTATGCCGATTCACTGAAGACAGG TTCACCATCTCCAGAGATGATTCAAAAACACTGCTTATCTACAAATGAACAACCTGAAAACTGA GGACACTGCCGTGTACTACTGTGAGACATGGAACTTCGGTAATAGCTACATACTACTGGG CTTACTGGGGCCAAAGGACTCTGGTACCGTCTCTCAGGTGGTGGTCTGGCGGGCGGCG TCCGTGGTGGTGGTCTCAGACTGTGACTCAGGAACCTTCACTACCGTATCACTGGTGG AACAGTCACACTCACTGTGGTCTCTCGACTGGGCTGTACATCTGGCAACTACCCAACTGGG TCCAAACAAAACAGGTCAGGCACCCCGTGTCTAATAGTGGGACTAAGTTCCTCGCCCCGGT ACTCTGCCAGATTCTCAGGCTCCCTGCTGGAGCAAGGTGCCCTCACCTCTCAGGGGTACA GCCAGAGGATGAGGCAGATAATTACTGTGTCTATGTTACAGCAACCGCTGGGTGGTGGAG GAACAAACTGACTGTCTA</p>
299.	CD33 E11 HL x H2C HL	artificial	<p>aa</p> <p>QVQLVQSGAEVKKPGESVKVSKASGYTFNYGMNWKQAPQGLEWMGWINTYGEPTYADKFKQ GRVTMTDTSTAYMEIRNLGGDDTAVYCARWSWDGYVYFDYWGQGTSTVIVSS9999999 9999999DIVMTQSPDSLTVSLGERTTINCKSSQSLDSTNKNLAWYQQKPGQPPKLLSWAS TRESGIPDRFSGSGSDFTLTIDSPQEDSATYVCOQSAHFPITFGQGTREIKSGSGSGSEVQL VESGGGLVQPGGSLKLSCAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYYADSVKDR FTISRDSKNTAYLQMNLLKTEDTAVYVCVRHGFNSYISYWAYWGQGTSTVIVSSGGSGGGG SGGGSGQTVVTOEPSLTVSPGGTTLTCGSSSTGAVTSGYYPNWWQKPGQAPRGLIGGTFKLAPG TPARFSGSLGGKAALTLSGVQPEDEAEYCALWYSNRWVFGGTKLTVL</p>
300.	CD33 E11 HL x H2C HL	artificial	<p>nt</p> <p>CAGGTGACGCTGGTGCAGTCTGGAGCTGAGTGAAAGACCTGGAGAGTCAGTCAAGGTCTCCTG CAAGCTAGCGGTATACCTTCACAACTATGGAATGAATGAACTGGTGAAGCAGGCTCCAGCACAGG GTTAGAGTGGATGGCTGGATAAACACCTACACTGAGAGCCAACTATGCTGATAGTCCAG GGACCGTTACCATGACTACGGATACCTCTACAGCACTGCCATATGGAATCCGCAACCTCGG AGGTGATGACACGGCTGTATATTACTGTGCGCTGGAGTGGAGTGTGTTACTACGTTTACT TTGACTACTGGGCGCAAGGCACTTCGGTCACTGCTCCCTCAGGTGGTGGTCTGGCGGGCGG GGCTCCGGTGGTGGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTGTCTCT GGCGAGAGGACCACTCAACTGCAAGTCCAGCAGAGTGTTTAGACAGCTCCACGAATAAGA ACTCCTTAGCTTGGTACCAGCAGAAACAGGACAGCTCTCTAAATTACTCTTCTCTGGGCATCT ACGCGGAATCCGGATCCCTGACCGATTCACTGGCAGCGGTCTGGACAGATTTCACCTCAC TATTGACAGCCCGCAGCCTGAAGATTCTGCACTTACTATTGTCAACAGTCTGCCCACTTCCCGA</p>

			<p>GGACACTGCCGTGTAAGTCTGTGTGAGACATGGAACCTTCGGTAATAGTACGTTTCCTGGTGGG CTTACTGGGGCCCAAGGACTCTGTGTACCGTCTCCTCAGGTGGTGGTCTTGGGGGGGGCGGC TCCGGTGGTGGTGGTCTCAGACTGTGTGACTCAGGAACCTTCACTCACCCTATCACCTGGTGG AACAGTCACACTCACTTGTGGCTCTGACTGGGCTGTATCATCTGGCAACTACCAAACTGGG TCCAACAAAACCAGGTAGGACCCCGTGGTCTAATAGTGGGACTAAGTTCCTGCCCCCGGT ACTCCTGCCAGATTCTCAGGCTCCCTGCTGGAGGCAAGGCTGCCCTCAOCCCTCAGGGGTACA GCCAGAGGATGAGGCAGAAATATTACTGTGTCTATGTGTATGTACAGCAACCGCTGGGTGTCGGTGGAG GAACCAAACTGACTGTCCTA</p>
303.	CD33 E11 HL x I2C HL	artificial aa	<p>QVQLVQSGAEVKKPGESVKVCKASGYTFITNYGMNWVKAPGQGLEWMGWINTYTGEPYADKFQ GRVTMTTDTSTSTAYMEIRNLGGDDTAVYCARWSWSDGYVYFDYWGQGTSTVTSVSSgggsggg gsgggsDIVMTQSPDSLTVSLGERITINCKSSQSVLDSSTNKNLSAWYQQKPGQPPKILLSWAS TRESGIPDRFSGSGSGTDFTLTIDSPQEDSATYCYQQSAHFPIITFGQGTREIKSGGGSEVQL VESGGGLVQPGGSLKLSCAAAGFTFNKYAMNWVRQAPGKLEWVARISKYNNVATYADSVKDR FTISRDSKNTAYLQMNLLKTEDTAVYICVRHGFNFSYISYWAYWGQGLTVTVSSGGGGSGGGG SGGGGQTVVTVQEPSTVSPGGTVTLTCSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPG TPARFSGSLGGKAAITLSGVQPEDEAEYICVLWYSNRWVFGGTKLTVL</p>
304.	CD33 E11 HL x I2C HL	artificial nt	<p>CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGTGAAGACCTGGAGAGTCAGTCAAGTCTCCTCG CAAGGCTAGCGGGTATACCTTCACAACTATGGAATGAAGTGGTGAAGCAGGCTCCAGGACAGG GTTTAGAGTGGATGGCTGGATAAACACCTACACTGGAGAGCCAACTATGCTGATAAAGTTCAG GGACGGTTACCATGACTACGGATACCTTACCAGCACTGCCATATATGGAATCCGCAACCTCGG AGGTGATGACACGGCTGTATATTACTGTGCGGCTGGAGTGGAGTATGGTTACTACGTTTACT TTGACTACTGGGGCCAAGGCATTCGGTCAACCGTCTCCTCAGGTGGTGGTCTGCGGGCGGC GGCTCCGGTGGTGGTCTTGACATCGTGATGACACAGTCCAGACTCCCTGACTGTCTCT GGCGGAGAGGACCAACCATCAACTGCAAGTCCAGCCAGAGTGTTTAGACAGCTCCACGAATAAGA ACTCCTTAGCTTGGTACCAGCAGAAACCAGGACAGCTCCTAAATTACTCCTTTCCTGGCATCT ACGCGGGAATCCGGATCCCTGACCGATTCAAGTGGCAGCGGTCTGGACAGATTTCATCTCAC TATTGACAGCCCGCAGCCTGAAGATTCTGCAACTTACTATTGTCAACAGTGTGCCACTTCCCGA TCACCTTTGGCCAAGGACACGACTGGAGATTAAATCCGGAGGTGGTGGTCCGAGGTGCAGTGG GTCGAGTCTGGAGGAGGATTGGTGCAGCCTGGAGGGTCAATTGAACTCTCATGTGCAGCCTCTGG ATTCACTTCAATAAGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAGGGTTTGGAAATGGG TTGCTCGCATAGAAGTAAATATAATATTATGCAACATATATGCCGATTTCAGTGAAGACAGG TTCACCATCTCCAGAGATGATTCAAAAAACAATGCCATCTACAAATGAACAACTTGAAAACTGA GGACACTGCCGTGTACTACTGTGTGAGACATGGGAACCTTCGGTAATAGCTACATATCCTACTGGG CTTACTGGGGCCCAAGGACTCTGGTCAACCGTCTCCTCAGGTGGTGGTCTTGGGGGGCGGGC TCCGGTGGTGGTGGTCTCAGACTGTTGTGACTCAGGAACCTTCACTCACCCTATCACCTGGTGG AACAGTCACACTCACTTGTGGTCTCCTGACTGGGCTGTIACATCTGGCAACTACCCAACTGGG TCCAACAAAACCAGGTAGGACCCCGTGGTGTATAGTGGGACTAAGTTCCTCGCCCCCGGT</p>

				ACTCCTGCCAGATTCTCAGGCTCCCTGCTTGGAGGCAAGGCTGCCCTCACCCTCTCAGGGGTACA GCCAGAGGATGAGGCAGAAATATTACTGTGTTCTATGTTACAGCAACCGCTGGGTGTTCCGGTGAG GAACCAAACTGACTGTCTTA
305.	CD33	human	nt	ATGGGATGGAGCTGTATCATCCTCTTCTTGTAGCAACAGCTACAGGTGTACACTCCGATCCAAA TTTCTGGCTGCAAGTGCAGGAGTCAGTACGGTACAGGAGGTTTGTGCTCTCTCGTGCCTGCA CTTTCTTCCATCCCATACCTACTACGACAACTCCCACTCATGGTTACTGGTTCCGGGAA GGAGCCATTATATCCGGGACTCTCCAGTGGCACAACAAGCTAGATCAAGAAGTACAGGAGA GACTCAGGGCAGATTCCGCCCTCTTGGGATCCAGTAGGAACAACCTGCTCCCTGAGCATCGTAG ACGCCAGGAGGAGGATAATGGTTTCATACTTCTTTCGATGGAGAGGAGTACCAATACAGT TACAAATCTCCCACTCTCTGTGCATGTGACAGACTTGACCCACAGGCCCAAAATCCTCATCCC TGGCACTTAGAACCCGCCACTCCAAAACCTGACCTGTCTGTCTCTGGGCTGTGACGAGG GAACACCCCGATCTTCTCTGTTGTAGTGTGCCCCACCTCCCTGGGCCAGGACTACTCAC TCCTCGGTGCTCATATCACCCACGGCCCCAGGACCAAGCACTGACCTGACCTGTACAGTGAA GTTCTGCTGGAGTGGTGTGACTACGGAGAGAACCATCCAGCTCAACGTACCTATGTTCACAGA ACCCAACAACCTGGTATCTTCCAGGAGATGGCTCAGGGAACAAGACACAGGAGGAGTGGTT CATGGGGCCATTGGAGGAGCTGGTGTACAGCCCTGCTGCTCTTGTCTCTGCTCATCTTCTT CATAGTGAAGACCCACAGAGGAAGCAGCAGCAGCAGTGGCAGGAATGACACCCACCTA CCACAGGTCAGCTCCCGAAACACAGAAAGTCCAAGTTACATGGCCCCACTGAAACCTCA AGCTGTTCAGGTGCCGCCCTACTGTGGAGATGGATGAGGAGTGCATTATGCTTCCCTCAACTT TCATGGGATGAATCCTTCCAAGGACCTCCACCGAATACTCAGAGTCCAGGACCCAGTCCGGGC ATCATCACCATCATATTGA
306.	CD33	human	aa	MGWSIIILFVATATGVHSDPNFWLQVQSVTVQEGLCVLVPCTFHFPIPYDKNSPVHCYWFRE GAIISGDSPVATNKLQDEVEETQGRFRLLGDP SRNNCSLSIVDARRRNGSYFFRMERGSTKYS YKSPQLSVHVTDLTHRPKILIPGTLEPGHKNLTC SVSWACEQGTPIFSWLSAAPTSLGPRTH SSVLIITPRPDHGTNLTCQVRFAGAGVTERTIQLNVTYVQNPTTGI FPGDGSQKQETRAGVW HGAIGGAGVTALLALCLCLIFFIVKTHRRKAARTAVGRNDTHPTTGSASPKHQKSKLHPTETS SCSGAAPTVMDEELHYASLNFHGMNPSKDTSTEYSEVRTQSGHHHHH
307.	CD33	macaque	nt	ATGCCGTGCTGCTACTGCTGCCCTGCTGTGGCAGGGGCCCTGGCTATGGATCCAGAGTCAG GCTGGAAGTGCAGGAGTCAGTGACAGTACAGGAGGGTTTGTGCTCTTGTGCCCTGCATTCT TCCATCCGTACCTACCAACACAGGAATCCCACTCATGGTTACTGTTCCGGGAAGGAGCC ATTGTATCCTTGACTCTCCAGTGGCCACAACAAGCTAGATCAAGAAGTACAGAGGAGACCCA GGGCGGATCCGCCCTCCTTGGGATCCAGTAGGAACAACCTGCTCCCTGAGCATCGTAGTGCCA GGAGAGGGATAACGGTTCACTACTTCTTCGGATGGAGAAAGGAGTACCAATACAGTTACAAA TCTACCCAGCTCTGTGATGTGACAGACTTGACCCACAGGCCCAATCCTCATCCTCCCTGGAGC CCTAGACCTTGACCACTCCAAAACCTGACCTGCTGTGCCCCCTGGGCTGTGAGCAGGGAACAC CTCCAATCTTCTCTGGAIGTCAGCTGCCCCCACTCCCTGGGCTCAGGACCACTCACTCCTCG GTGTCATATATACCCCAAGGCCCCAGGACCCAGGCAACCTCACCCTGTGAGGTGAGTTCCC

308.	CD33	macaque	aa	<p>TGGAGCTGGGTGACCGAGAGAACCATCCAGCTCAATGTCTCCTATGCTTACAGAACCCAA GAACTGATATCTTTCTAGGAGACGGCTCAGGAAACAGGAGTGGTTCAGGAGCCATCGGGGA GCTGTGTACAGTCTCGTCTCTTTGTCTCTGCTCATCTTCTACAGTGAAGACTACAG GAGAAAGCAGCCAGGACAGCAGTGGCAGGATCGAACCCACCCGACAGGCGCAACATCCT CGAACACAGAGAAAGTCCAAAGTTACATGGCGCACTGAAACCTCAGGCTGTTACAGTACACCC CTTACTGTGAGATGATGAGGAGCTGCACCTACGCTTCCCTCAACTTTCATGGGATGAATCCTTC TGAGGACACCTCCACCGAATACTCAGAGGTCAGGACCCAGTGA</p> <p>MPLLLLLLWAGALAMDPRVRLEVQESVTVQEGLCVLPCTFFHFPVHYTRNSPVHGYWFREGA IVSLDSPVATNKLIDQEVQEEETQGRFRLLDPSRNNCSLSIVDARRRDNNGSYFFRMEKGSYK STQLSVHVTDLTHRPQILIPGALDPDHSKNLTCVSPWACEQGTPIFSWMSAAPTSLGLRTHSS VLIITPRPDHGTNLTCQVKFPAGVTTERTIQLNVSYASQNPRTDIFLDGSGKGQGVQGAIGG AGVTVLLALCLLIFFTVKTHRRKAARTAVGRIDTHPATGPTSSKHQKSKLHGATEITSGSGTT LTVEMDEELHYASLNFHGMNPSEDITSTEYSEVRTQ</p>
309.	1-27 CD3-Fc + Leader	artificial	nt	<p>ATGGGATGGAGCTGTATCATCTCTCTTCTGGTAGCAACAGCTACAGGTGTACACTCCCAAGATGG TAATGAGAAATGGGTGATATTACACAGACACCATATAAAGTCTCCATCTCTGGAACCAAGTAA TATTGACATCCGGAGAGCCCAATCTTGTGACAAAACCTACACATGCCACCGTCCCGACGACCT GAACTCCTGGGGACCGTCAGTCTTCTCTTCCGCCAAAACCCAAAGACACCTCATGATCTC CCGACCCCTGAGGTACATGCGTGTGGTGGTGCATATGCAAGACAAAGCCGGAGGAGTACAAAC ACTGTTACGTGACGGGTGGAGTGCATATGCAAGACAAAGCCGGGAGGAGTACAAAC AGCACGTACCGTGTGGTCAAGTCTCTCACCGTCTGCAACAGGACTGGTGAATGGCAAGAGTA CAAGTGCAAGGTCTCCAAACAAGCCCTCCAGCCCGCCATCGAGAAACCATCTCCAAAGCCAAAG GGCAGCCCGAGAACACAGGTGTACACCTGCCCGCCATCCCGGAGGAGATGACCAAGAACCCAG GTCAGCCTGACCTGCTGTTCAAAGCTTCTATCCAGCGACATCGCCGTGGAGTGGGACAGCAA TGGGACGCGGAGAACAACTACAAGACACCGCTCCGTGCTGGACTCCGACGGCTCCTCTCTCC TCTATAGCAAGCTCACCGTGGACAAAGAGCAGGTGGCAGCAGGGGAAACGCTTCTCTGCTCCGTG ATGATGAGGCTCTGCACAACTACACGACAGAGAGCTCTCCCTGTCCCGGGTAAATAG</p> <p>MGWSCTILFLVATATGVHSQDNGNEEMGGITQTPKYVSIISGTTVILTSGEPKSCDKTHTCPPCPAP ELLGGPSVFLFPKPKDITLMSRTPEVTCVVVDVSHEDPEVKENWYVDGVEVHNAKTKPREEQYN STYRVSVLTIVLHQDLNGKEYKCKVSNKALPAPIEKTIISKAKGQPREPQVYITLPPSREMTKNQ VSLTCLVKGFIYPSDIAVEWESNGQPENNYKTTTPVLDSDGSEFFLYSKLTVDKSRWQQGNVPSV MHEALHNHYTQKSLSLSPGK</p>
310.	1-27 CD3-Fc + Leader	artificial	aa	<p>EVQLVDSGGGLVQPGGSLKLSKAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNVATYYADS VKDRFTLSRDDSKNTAYLQMNLLKTEDTAVYCVRHGFGNSYISYWAYWGQGLTVTVSSGGGGS GGGGSGGGSQTVVTOEPSTLTVSPGGTTLTCSSTGAVTSYYPNWWQKPGQAPRGLIGGTFK LAPGTPARESGSLGKKAALTLGVPQDEAEYCYCALWYSNRWVEGGGKLTIVLSGGGGSQVQLV QSGAEVKKPKASVKVSKASGYTFTNYGMNWVKQAPGQGLKWMGWINTYTGEPYADDFKGRVTM TSDTSTSTAYLELHNLRSDDTAVYYCARWSWSDGYIVYFDYWQGTITVTVSSGGGGSGGSGGG</p>
311.	CD33 UD H2C HL x AF5 HL	artificial	aa	

312.	CD33 UD H2C HL x AF5 HL	artificial	nt	<p>GSDIVMTQSPDLSLTVSLGERTTINCKSSQSVLDSSKNKNSLAWYQOKPQPPLKLLSWASTRESG IPDRFSGSGSGTDFTLTIDSLQPEDSATYYCQOQSAHFPIITFGQGTRLEIK</p> <p>GAGGTGCAGCTGGTCGAGTCTGGAGGAGGATTGGTCAGCCTGGAGGGTCAATTGAAACTCTCATG TGCAGCCTCTGGATTCAACCTTCAATAAGTACGCCATGAACTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAAATATAATAATATGCAACATATATGCGCGATTCA GTGAAGACAGGTTACCATCTCCAGAGATGATTCAAAAACACTGCCTATCTACAAATGAACAA CTTGAATACTGAGGACACTGCCGTGTACTGTGTGAGACATGGAACTTCGGTAATAGCTACA TATCCTACTGGGCTTACTGGGGCCAAAGGACTCTGGTCACCGTCTCTCAGGTGGTGGTGTCT GGCGGGCGGCTCCGGTGGTGGTGTCTCAGACTGTGTGACTCAGGAACCTTCACTCACCGT ATCACCTGGTGAACAGTCACTCACTTGTGGTCTCTCGACTGGGCTGTACATCTGGTACT ACCAAACCTGGTCCAAACAAACAGGTCAAGCACCCCGTGGTCTAATAGGTGGGACTAAGTTT CTGCCCCCGGTACTCTCTGCCAGATTCTCAGGCTCCCTGCTTGGAGCAAGGCTGCCCTCACCT CTCAGGGTACAGCCAGAGATGAGGCAGAAATATTACTGTGCTCTATGTTACAGCAACCCGTGGG TGTTCGGTGGAGAACCAAACTGACTGTCTCTATCCGGAGGTGGTGGTCCCAGGTGCAGCTGGTC CAGTCTGAGCTGAGTGAAGAGCTGGAGCTCAGTCAAGTCTCTGCAAGCTAGCGGTA TACCTCACAAACTATGGAATGAAGTGGTGAAGCAGGCTCCAGGACAGGTTTAAAGTGGATGG GCTGATATAACACCTACACTGGAGAGCCACATATGCTGATGACTCAAGGACGGGTACCATG ACTTCGGATACCTCTACCAGCACTGCCTATTTGGAACTCCACAACCTCAGAAGTATGACACGGC TGATATATTACTGTGGCGCTGGAGTGGAGTATGTTACTACGTTTACTTGTACTACTGGGGCC AAGCACTACGGTCAACCGTCTCTCAGGTGGTGGTGGTCTTGGCGGGCGGGCTCCGGTGGTGGT GGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTCTCTGGCGAGAGGACCAC CATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCAAGATAAGAACTCCTTAGCTTGGT ACCAGCAGAAACCCAGGACAGCTCCTAAATTACTCCTTTCCTGGGACATCAGCGGGAAATCCGGG ATCCTTGACCGATTCAGTGGCAGCGGTCTGGGACAGATTTCACCTCACTATTGACAGCCTGCA GCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCCACTTCCCGATCACCTTTGGCCAAAG GGACACGACTGGAGATTAAA</p> <p>EVQLVESGGGLVQPGGSLKLSCAASGFTFNSYAMNWVRAQPKGLEWVARIRSKYNNYATYYADS VKGRFTISRDDSKNTAYLQMNNLKTEDTAVYCYVRHGFGNSYVSWWAYWGQGLTVTVSSGGGS GGGSGGGGSGQTVTVTQEPSLTVSPGGTVTLTCCSGTGAFTSGNYPNWVQKPGQAPRGLIGTKF LAPGTPAREFSGSLGGKAALTLSGVQPEDEAEYCYVLWYNSNRWVFGGKLTIVLSGGGGSQVQLV QSGAEVKKPGASVKVSKASGYTFITNYGMNWVKQAPGQGLKWMGWINTYTGEPTYADDFKGRVTM TSDTSTSTAYLELHLNLRSDDTAVYYCARWSWSDDGYVYFYDWGQGTIVTVSSGGGSGGGSGGGG GSDIVMTQSPDLSLTVSLGERTTINCKSSQSVLDSSKNKNSLAWYQOKPQPPLKLLSWASTRESG IPDRFSGSGSGTDFTLTIDSLQPEDSATYYCQOQSAHFPIITFGQGTRLEIK</p> <p>GAGGTGCAGCTGGTCGAGTCTGGAGGAGGATTGGTCAGCCTGGAGGGTCAATTGAAACTCTCATG TGCAGCCTCTGGATTCAACCTTCAATAAGTACGCCATGAACTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAAATATAATAATATGCAACATATATGCGCGATTCA GTGAAGACAGGTTACCATCTCCAGAGATGATTCAAAAACACTGCCTATCTACAAATGAACAA CTTGAATACTGAGGACACTGCCGTGTACTGTGTGAGACATGGAACTTCGGTAATAGCTACA TATCCTACTGGGCTTACTGGGGCCAAAGGACTCTGGTCACCGTCTCTCAGGTGGTGGTGTCT GGCGGGCGGCTCCGGTGGTGGTGTCTCAGACTGTGTGACTCAGGAACCTTCACTCACCGT ATCACCTGGTGAACAGTCACTCACTTGTGGTCTCTCGACTGGGCTGTACATCTGGTACT ACCAAACCTGGTCCAAACAAACAGGTCAAGCACCCCGTGGTCTAATAGGTGGGACTAAGTTT CTGCCCCCGGTACTCTCTGCCAGATTCTCAGGCTCCCTGCTTGGAGCAAGGCTGCCCTCACCT CTCAGGGTACAGCCAGAGATGAGGCAGAAATATTACTGTGCTCTATGTTACAGCAACCCGTGGG TGTTCGGTGGAGAACCAAACTGACTGTCTCTATCCGGAGGTGGTGGTCCCAGGTGCAGCTGGTC CAGTCTGAGCTGAGTGAAGAGCTGGAGCTCAGTCAAGTCTCTGCAAGCTAGCGGTA TACCTCACAAACTATGGAATGAAGTGGTGAAGCAGGCTCCAGGACAGGTTTAAAGTGGATGG GCTGATATAACACCTACACTGGAGAGCCACATATGCTGATGACTCAAGGACGGGTACCATG ACTTCGGATACCTCTACCAGCACTGCCTATTTGGAACTCCACAACCTCAGAAGTATGACACGGC TGATATATTACTGTGGCGCTGGAGTGGAGTATGTTACTACGTTTACTTGTACTACTGGGGCC AAGCACTACGGTCAACCGTCTCTCAGGTGGTGGTGGTCTTGGCGGGCGGGCTCCGGTGGTGGT GGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTCTCTGGCGAGAGGACCAC CATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCAAGATAAGAACTCCTTAGCTTGGT ACCAGCAGAAACCCAGGACAGCTCCTAAATTACTCCTTTCCTGGGACATCAGCGGGAAATCCGGG ATCCTTGACCGATTCAGTGGCAGCGGTCTGGGACAGATTTCACCTCACTATTGACAGCCTGCA GCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCCACTTCCCGATCACCTTTGGCCAAAG GGACACGACTGGAGATTAAA</p>
313.	CD33 UD F12Q HL x AF5 HL	artificial	aa	<p>EVQLVESGGGLVQPGGSLKLSCAASGFTFNSYAMNWVRAQPKGLEWVARIRSKYNNYATYYADS VKGRFTISRDDSKNTAYLQMNNLKTEDTAVYCYVRHGFGNSYVSWWAYWGQGLTVTVSSGGGS GGGSGGGGSGQTVTVTQEPSLTVSPGGTVTLTCCSGTGAFTSGNYPNWVQKPGQAPRGLIGTKF LAPGTPAREFSGSLGGKAALTLSGVQPEDEAEYCYVLWYNSNRWVFGGKLTIVLSGGGGSQVQLV QSGAEVKKPGASVKVSKASGYTFITNYGMNWVKQAPGQGLKWMGWINTYTGEPTYADDFKGRVTM TSDTSTSTAYLELHLNLRSDDTAVYYCARWSWSDDGYVYFYDWGQGTIVTVSSGGGSGGGSGGGG GSDIVMTQSPDLSLTVSLGERTTINCKSSQSVLDSSKNKNSLAWYQOKPQPPLKLLSWASTRESG IPDRFSGSGSGTDFTLTIDSLQPEDSATYYCQOQSAHFPIITFGQGTRLEIK</p> <p>GAGGTGCAGCTGGTCGAGTCTGGAGGAGGATTGGTCAGCCTGGAGGGTCAATTGAAACTCTCATG TGCAGCCTCTGGATTCAACCTTCAATAAGTACGCCATGAACTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAAATATAATAATATGCAACATATATGCGCGATTCA GTGAAGACAGGTTACCATCTCCAGAGATGATTCAAAAACACTGCCTATCTACAAATGAACAA CTTGAATACTGAGGACACTGCCGTGTACTGTGTGAGACATGGAACTTCGGTAATAGCTACA TATCCTACTGGGCTTACTGGGGCCAAAGGACTCTGGTCACCGTCTCTCAGGTGGTGGTGTCT GGCGGGCGGCTCCGGTGGTGGTGTCTCAGACTGTGTGACTCAGGAACCTTCACTCACCGT ATCACCTGGTGAACAGTCACTCACTTGTGGTCTCTCGACTGGGCTGTACATCTGGTACT ACCAAACCTGGTCCAAACAAACAGGTCAAGCACCCCGTGGTCTAATAGGTGGGACTAAGTTT CTGCCCCCGGTACTCTCTGCCAGATTCTCAGGCTCCCTGCTTGGAGCAAGGCTGCCCTCACCT CTCAGGGTACAGCCAGAGATGAGGCAGAAATATTACTGTGCTCTATGTTACAGCAACCCGTGGG TGTTCGGTGGAGAACCAAACTGACTGTCTCTATCCGGAGGTGGTGGTCCCAGGTGCAGCTGGTC CAGTCTGAGCTGAGTGAAGAGCTGGAGCTCAGTCAAGTCTCTGCAAGCTAGCGGTA TACCTCACAAACTATGGAATGAAGTGGTGAAGCAGGCTCCAGGACAGGTTTAAAGTGGATGG GCTGATATAACACCTACACTGGAGAGCCACATATGCTGATGACTCAAGGACGGGTACCATG ACTTCGGATACCTCTACCAGCACTGCCTATTTGGAACTCCACAACCTCAGAAGTATGACACGGC TGATATATTACTGTGGCGCTGGAGTGGAGTATGTTACTACGTTTACTTGTACTACTGGGGCC AAGCACTACGGTCAACCGTCTCTCAGGTGGTGGTGGTCTTGGCGGGCGGGCTCCGGTGGTGGT GGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTCTCTGGCGAGAGGACCAC CATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCAAGATAAGAACTCCTTAGCTTGGT ACCAGCAGAAACCCAGGACAGCTCCTAAATTACTCCTTTCCTGGGACATCAGCGGGAAATCCGGG ATCCTTGACCGATTCAGTGGCAGCGGTCTGGGACAGATTTCACCTCACTATTGACAGCCTGCA GCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCCACTTCCCGATCACCTTTGGCCAAAG GGACACGACTGGAGATTAAA</p>
314.	CD33 UD F12Q HL x AF5 HL	artificial	nt	<p>GAGGTGCAGCTGGTCGAGTCTGGAGGAGGATTGGTCAGCCTGGAGGGTCAATTGAAACTCTCATG TGCAGCCTCTGGATTCAACCTTCAATAAGTACGCCATGAACTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTGCTCGCATAGAAGTAAATATAATAATATGCAACATATATGCGCGATTCA GTGAAGACAGGTTACCATCTCCAGAGATGATTCAAAAACACTGCCTATCTACAAATGAACAA CTTGAATACTGAGGACACTGCCGTGTACTGTGTGAGACATGGAACTTCGGTAATAGCTACA TATCCTACTGGGCTTACTGGGGCCAAAGGACTCTGGTCACCGTCTCTCAGGTGGTGGTGTCT GGCGGGCGGCTCCGGTGGTGGTGTCTCAGACTGTGTGACTCAGGAACCTTCACTCACCGT ATCACCTGGTGAACAGTCACTCACTTGTGGTCTCTCGACTGGGCTGTACATCTGGTACT ACCAAACCTGGTCCAAACAAACAGGTCAAGCACCCCGTGGTCTAATAGGTGGGACTAAGTTT CTGCCCCCGGTACTCTCTGCCAGATTCTCAGGCTCCCTGCTTGGAGCAAGGCTGCCCTCACCT CTCAGGGTACAGCCAGAGATGAGGCAGAAATATTACTGTGCTCTATGTTACAGCAACCCGTGGG TGTTCGGTGGAGAACCAAACTGACTGTCTCTATCCGGAGGTGGTGGTCCCAGGTGCAGCTGGTC CAGTCTGAGCTGAGTGAAGAGCTGGAGCTCAGTCAAGTCTCTGCAAGCTAGCGGTA TACCTCACAAACTATGGAATGAAGTGGTGAAGCAGGCTCCAGGACAGGTTTAAAGTGGATGG GCTGATATAACACCTACACTGGAGAGCCACATATGCTGATGACTCAAGGACGGGTACCATG ACTTCGGATACCTCTACCAGCACTGCCTATTTGGAACTCCACAACCTCAGAAGTATGACACGGC TGATATATTACTGTGGCGCTGGAGTGGAGTATGTTACTACGTTTACTTGTACTACTGGGGCC AAGCACTACGGTCAACCGTCTCTCAGGTGGTGGTGGTCTTGGCGGGCGGGCTCCGGTGGTGGT GGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTCTCTGGCGAGAGGACCAC CATCAACTGCAAGTCCAGCCAGAGTGTTTTAGACAGCTCCAAGATAAGAACTCCTTAGCTTGGT ACCAGCAGAAACCCAGGACAGCTCCTAAATTACTCCTTTCCTGGGACATCAGCGGGAAATCCGGG ATCCTTGACCGATTCAGTGGCAGCGGTCTGGGACAGATTTCACCTCACTATTGACAGCCTGCA GCCTGAAGATTCTGCAACTTACTATTGTCAACAGTCTGCCCACTTCCCGATCACCTTTGGCCAAAG GGACACGACTGGAGATTAAA</p>

<p>GTGAAAGGCAGGTTACCATCTCCAGAGATGATTCAAAAAACACTGCTATCTACAAATGAACAA CTTCAAAACTGAGGACACTCCCGTGTACTACTGTGTGAGACATGGGAACCTCGGTAATAGCTACG TTTCTGTGTGGCTTACTGGGCCAAGGACTCTGGTCACCGTCTCCTCAGGTGGTGGTTCT GGCGGGCGGCTCCGGTGGTGGTGTCTCAGACTGTGTGACTCAGGAACCTTCACTCACCGT ATCACCTGTGGAACAGTCACACTCACTTGTGGCTCTCAGCTGGGCTGTACATCTGGCAACT ACCCAACTGGTCCAAACAAACACAGGTCAAGCAACCGCTGGTCTAATAGTGGGACTAAGTTT CTGCCCCCGTACTCTGCCAGATTCTCAGGCTCCCTGCTGGAGGCAAGGCTGCCCTCACCT CTCAGGGTACAGCCAGAGGATGAGGAGAAATTAATCTGTGTCTAATAGTGGGCAAGGCTGCCCT TGTTCCGGTGAGGAACCAAACTGACTGCTCTATCCGAGGTGGTGGCTCCAGGTGCAGCTGGTC CAGTCTGAGCTGAGGTGAAGAAGCTGGAGCGTCACTCAAGGCTCTGCAAGGCTAGCGGTA TACCTTCAAACTATGGAATGAACCTGGGTGAAGCAGGCTCCAGACAGGCTTAAAGTGGATGG GCTGGATAAACACCTACACTGGAGAGCCAAACATATGATGACTCAAGGACGGTTACCATG ACTTCGGTACCTCTACCAGCACTGCCCTATTGGAACTCCACAACTCAGAAGTATGACACGGC TGTATATACTGTCGGCGTGGAGTTGGAGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGT AAGGCACTACGGTCACCGTCTCCTCAGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGT GGTCTGACATCGTGATGACACAGTCTCCAGACTCCCTGACTGTCTCTGGCGAGAGGACAC CATCACTGCAAGTCCAGCAGAGTGTCTTAGACAGTCCAAAGTAAAGAACTCCTTAGCTTGGT ACCAGCAAAACAGGACAGCTCTCTAAATTAATCTCTCTGGCATCTACGCGGAATCCGGG ATCCCTACCGATTCACTGGCAGCGCTCTGGGACAGATTCACTCTCACTATTGACAGCTGCA GCCTGAGATTCTGCAACTTACTATTGTCAACAGTCTCCCACTTCCCGATCACCTTTGGCCAAAG GGACACGACTGGAGATTAA</p>			
<p>315.</p>	<p>CD33 UD I2C HL x AF5 HL</p>	<p>artificial</p>	<p>aa</p>
<p>EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYYADS VKDRFTISRDDSKNTAYLQMNLLKTEDTAVYYCVRHGNGFNSYISWAYWGQGLTVTVSSGGGS GGSGGGGQTVVTVQEPSTLTVSPGTVTLTCGSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFK LAPGTPARFSGSLLGKAAALTLGVQPEDEAEYCYVLWYSNRWVFGGKLTLSGGGGSQVQLV QSGAEVKKPGASVKVSKASGYFTNYGMNWVKQAPQGLKWMGWINTYTGEPTYADDFKGRVTM TSDTSTAYLELHNLRSDDTAVYYCARWSWSDGYVYFDYWGQGTITVTVSSGGGSGGGSGGG GSDIVMTQSPDSLTVSLGERTTINCKSSQSVLDSKKNKSLAWYQQKPCQPPLKLLSWASTRESG IPDRFSGSGSTDFLTITIDSLQPEDSATYYCQQAQSAHFPIITFGQTRLEIK</p>		<p>nt</p>	
<p>316.</p>	<p>CD33 UD I2C HL x AF5 HL</p>	<p>artificial</p>	

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<p>GTACGCCATGAACCTGGGTCCGCCAGGCTCCAGGAAAGGGTTTGGAAATGGGTGCTCGCATAAGAA GTAATATAATAATATGCAACATATTATGCCGATTATGCGGATTCAGTGAACACAGGTTACCATCTCCAGA GATGATCAAAAAACACTGCCTATCTACAAATGAACAACTTGAAGAACTGAGGACACTGCCGTGTA CTACTGTGAGACATGGAACTTCGTAATAGTACATATCCTACTGGGCTTACTGGGCCAAG GGACTCTGGTACCGTCTCCTCAGTGGTGGTCTGGCGGGCGGCTCCGGTGGTGGT TCTCAGACTGTGTGACTCAGGAACCTTCACTACCGTATCACTGGTGAACAGTACACTCAC TTGTGGTCTCTGACTGGGCTGTACATCTGGCTACTACCAAACTGGTCCAAACAAACAG GTCAGGCACCCCGTGGTCTAATAGTGGGACTAAGTTCCTCGCCCCGGTACTCTGCCAGATTC TCAGGTCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGTACAGCCAGGATGAGGC AGAATATTACTGTGCTCTATGGTACAGCAACCGCTGGGTGTGGTGGAGAACCAACTGACTG TCCTA</p>	<p>QVQLVSGAEVKKPGASVKVSCKASGYPTGYMHVWRQAPGGLEWMGWINPNSGGTNYAQKFQ GRVTITADESTAYMELSRSDDTAVYYCAKSWFASWGQTIVTVSSGGSGGGSGGG GSDIVMTQSPDLSAVSLGERATINCKSSQSVLSSNNKYNLWYQQKPKLLIYWASTRESG VPDRFSGSGTDFTLTISSLQAEADVAVYCCQHFNTPEAFQGTGLEIKSGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNSYAMNWRQAPGKLEWVARIRSKYNNYATYYADSVKGRFTISR DDSKNTAYLQMNNLKTEDAVYYCVRHGNFGNSYVSWAYWQGTIVTVSSGGSGGGSGGGG SQTVVTEPSLTIVSPGTVTLTICGSSSTGAVTSNYPNWPQKPGAPRGLIGGTFKFLAPGTPARF SGSLLGKKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGKLTVL</p>	<p>CAGTGCAGCTGGTCCAGTCTGGGCTGAGGTGAAGAGCTGGGCGCTCAGTGAAGTCTCCTG CAAGGCTCTGGATACCCCTTACCGGCTACTACATGCTGGTGGACAGGCCCTGGACAAG GGCTGAGTGGATGGATGATCAACCCCTAACAGTGTGGCACAACTATGCACAGAAGTTTCAG GGCAGAGTCAGGATACCGCGGACGAATCCACGAGCACAGCTACATGGAGCTGAGCAGGCTGAG ATCTGACGACACGGCGGTGATTAATGTCGGAATCCTGGTCTCTGGTCTCTGGTCTCTGGTCT AAGGAACCTGGTCAACGCTCTCCTCAGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGT GGTCTGACATCTGTGATGACACAGTCTCCAGACTCCCTGGTGTGTCTGGCGAGAGGGCCAC CATCACTGCAAGTCCAGCCAGAGTGTCTTATCCAGCTCCAAACAATAAGAACTACTTAAATTGGT ACCAGCAAAACAGGACAGCCTCCTAAGTTGCTCAATTTAGGCACTACCCGGGAATCCGGG GTCCCTGACCGATTGAGTGGCAGGGGTCTGGGACAGATTTCACTCTACCATCAGCAGCCTGCA GGCTGAAGATGTGGCGGTTTATTACTGTCAACAACATTTAATACTCCGTTCTGCTTTGGCCAGG GGACCAAGCTGCAGATCAATCCGAGGTGGTGGATCCGAGGTGACGTGGTGGTCTGGAGGA GGATTGGTGCAGCCTGGAGGTCATTGAAACTCTCATGTGAGCCTCTGGATTCACCTTCAATAG CTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGGTTTGAATGGGTGGTCTGCATAAGAA GTAATATAATAATATGCAACATATTATGCCGATTGAGTGAAGCAGGTTTACCATCTCCAGA GATGATCAAAAAACACTGCCCTATCTACAAATGAACAACCTTGAACACTGAGGACACTGCCGTGTA CTACTGTGAGACATGGAACTTCGGTAATAGTACGTTCTCTGGTGGCTTACTGGGGCCAAAG GGACTCTGGTCAACGCTCTCCTCAGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGTGGT</p>
<p>319. MCSP-A9 HL x F12Q HL</p>	<p>aa artificial</p>	<p>nt</p>
<p>320. MCSP-A9 HL x F12Q HL</p>	<p>artificial</p>	<p>nt</p>

<p>321.</p>	<p>MCSP-A9 HL x l2C HL</p>	<p>artificial</p>	<p>aa</p>	<p>nt</p>	<p>TCTCAGACTGTTGTGACTCAGGAACCTTCACTCACCGTATCACCTGGTGGAACTCAGCTCAC TTGTGGCTCTCGACTGGGGCTGTATACATCTGGCAACTACCAAACTGGGTCCAACAAAACCCAG GTCAGGCACCCCGTGGTCTAATAGGTGGACTAAGTTCTCGCCCGGTACTCTGCCAGATTC TCAGGCTCCCTGCTGGAGGCAAGGCTGCCCTCACCCCTCAGGGGTACAGCCAGAGGATGAGGC AGAAATATTACTGTGTCTATGGTACAGCAACCGCTGGGTGTTCCGGTGGAGGAACCAAACTGACTG TCCTA</p> <p>QVQLVQSGAEVKFPGASVKVSKASGYPTGYMHVWRQAPGGGLEWMGWINPNSGGTNYAQKFQ GRVTITADESTAYMELSLRLSRDSDTAVYYCAKSWVFWFASWGQTLVTVSSGGSGGGSGGG GSDIVMTQSPDSLAVSLGERATINCKSSQSVLSSNNKNLWYQKPGQPPKLLIYWASTRESG VPDRFSGSGGTDFLTISLQAEDVAVYYCQGHFNTPEAFGGQTKLEIKSGGGGSEVQLVESGG GLVQPGSLKLSCAASGFTFNKYAMNWRQAPGKGLWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNLLKTEDTAVYYCVRHGNGNSYI SYWAYWGQTLVTVSSGGSGGGSGGGG SQTIVTQEPSLTVSPGGTTLTCSGSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTPARF SGSLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGTKLTVL</p> <p>CAGGTGCAGCTGGTCCAGTCTGGGGCTGAGGTGAAGAGCCTGGGGCTCAGTGAAGGTCTCCTG CAAGGCTTCTGGATACCCCTTACCGGCTACTACATGCATCTGGTGGCAGAGCCCTGGACAAG GGCTTGAGTGGATGGGATGATCAACCCCTAACAGTGGTGGCAAACTATGCACAGAAGTTTCAG GGCAGATCACGATTACCGCGGACGAATCCACGAGCACAGCTACATGGAGCTGAGCAGGCTGAG ATCTGACGACACGGCCGTGTATTACTGTGCGAAATCTGGGTCTCTGGTTTCTCTGGGGTC AAGGAACCTTGGTACCGTCTCTCAGGTGGTGGTGTCTGGGGGGGGGGTCCGGTGGTGGT GGTCTGACATCGTGTGACACAGTCTCCAGACTCCCTGGTGTGTCTCTGGCGAGAGGGCCAC CATCAACTGCAAGTCCAGCCAGAGTGTCTTATCCAGCTCCACAAATAAGAACTACTTAAATTGGT ACCAGCAGAAACCCAGGACAGCCTCCTAAGTTGCTATTACTGGGCATCTACCCGGGAATCCGGG GTCCCTGACCGATTCAAGTGGCAGGGTCTGGGACAGATTTCACTCTCAACATCAGCAGCCTGCA GGCTGAAGATGTGGCGGTTTATTACTGTCAACAACATTTTAACTCCGTTCGTCTTGGCCAGG GGACCAAGCTGGAGATCAAAATCCGAGGTGGTGGATCCGAGGTGCAGTGGTCTGAGTCTGGAGGA GGATTGGTGCACTGGAGGTCATTGAAACTCTCATGTGAGGCTCTGGATTACCTTCAATAA GTACGCCATGAATGGGTCGCCAGGCTCCAGGAAAGGTTTGAATGGGTGCTCGCATAGAA GTAATATAATAATATGCAACATATTATGCCGATTTCAGTGAAGACAGAGTTTCACTCTCCAGA GATGATTCAAAAACACTGCCCTATCTACAAATGAACAACCTTGAATACTGAGGACACTGCCGTGA CTACTGTGTGAGACATGGGAACCTTCGGTAATAGTACATATCTACTGGGCTTACTGGGGCCAAG GGACTCTGGTCAACGCTCTCTCAGGTGGTGGTGTCTGCGCGGCGGCTCCGGTGGTGGTGGT TCTCAGACTGTTGTGACTCAGGAACCTTCACTACCCGTATCAGTGGTGGAACTACACTCAC TTGTGGCTCTCTGACTGGGCTGTACATCTGGCAACTACCCAACTGGGTCCACAAAAACCCAG GTCAGGCACCCCGTGGTCTAATAGGTGGGACTAAGTTCCTCGCCCCGGTACTCTGCCAGATTCT TCAGGCTCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGC AGAAATATTACTGTGTCTATGGTACAGCAACCGCTGGGTGTTCCGGTGGAGGAACCAAACTGACTG</p>
<p>322.</p>	<p>MCSP-A9 HL x l2C HL</p>	<p>artificial</p>	<p>nt</p>		

323.	MCSP-C8 HL x l2C HL	artificial	aa	<p>TCCTA</p> <p>QVQLVQSGAEVKRPGASMKVSKASGYFTFTNYIHWVRQAPGGGLEWMGWINPNSGATNYAQKFQ GRVTMTTRDTSTVYMELSSLRSEDTAVYYCAKSWSFASWGQGTlVTVSSGGSGGGSGGG GSDIVMTQSPDSLAVSLGERATINCKSSQSVLNSKNNRNYLAWYQQKPGQPPKLLIYWASTRESG VPDRFSGSGSGTDFTLTISGLQAEDVAVYCCQHYSTPFTFGTKVDIKSGGGSEVQLVESGG GLVQPGSLKLSCAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYADSVKDRFTISR DDSKNTAYIQMNNLKTEDAVYYCVRHGNEGNSYISYMAVWGQTLVTVSSGGSGGGSGGGG SQTVTQEP SLTVSPGGTVTLTCSGSTGAVTSGNYPNWQQKPGQAPRGLIGGTFKFLAPGTPARF SGSLIGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGKILTVL</p> <p>CAGGTCCAGCTGGTCCAGTCTGGGCTGAGGTGAAGAGGCTGGGCTCAATGAAGGTCTCCTG CAAGGCTTCTGGGTACACCTTCACCAACTACTATATACACTGGGTGCGACAGGCCCTGGACAAG GTCTTGAAGTGGATGGGTGGATCAACCCCTAACAGTGGTGCACAAACTATGCACAGAAGTTCCAG GGCAGAGTCACCATGACCAGGACACGTCACAGCAGTCTACATGGAGCTGAGCAGCCTGAG ATCTGAGGACACGGCCGTGTTACTGTGCGAAATCTGGGTCTCTGGGTCTCTGGGTGGTGGT AAGAACCTTGGTCAACGCTCTCTCAGGTGGTGGTCTGGGCGAGAGGCCAC GGTTCGACATCGTGATGACCCAGTCTCCAGCTCCCTGGCTGTGTCTCTGGCGAGAGGCCAC CATCAACTGCAAGTCCAGCCAGAGTGTTTAAACAGCAGACAAATAGGAACACTAGCTTGGT ACGACAGAAACCAGGACAGCTCTTAAGTCTCTTACTGGGCTCTACCCGGAATCCGGG GTCCCTGACCGATTGAGTGGCAGCGGTCTGGGACAGATTCTACCTCAGTGGCTGCA GGCTGAAGATGTGGCAGTTTATTCTGTGACCAACATTAAGTACTCCATTCATTTGGCCCTG GGACCAAGTGGATATCAAAATCCGAGGTGGTGGATCCAGGTGAGCTGTGGATTCACCTTCAATAA GGATTGGTGCAGCTGGAGGTGCTTGAACCTCTCATGTGCGAGCTGTGGATTCACCTTCAATAA GTACGCCATGAAGTGGTCCGCCAGCTCCAGGAAAGGTTTGAATGGTGTGTCGCATTAAGAA GTAATATAATAATATGCAACATATATGCGGATTGAGTGAAGGAGAGGTTCAACATCTCCAGA GATGATTCAAAAACACTGCCTATCTACAAATGAACACTGAAAACTGAGGACACTGCCGTGTA CTACTGTGACACATGGAACTTCGGTAATAGCTACATATCTTACTGGGCTTACTGGGCGCAAG GGACTGTGTCACCGTCTCTCAGGTGGTGGTGTCTGGCGGCGGCTCCGGTGGTGGTGGT TCTCAGACTGTGTGACTCAGGAACCTTCACACCCGTAACCTGGTGGACAGTCAACACTCAC TTGTGGCTCCTCGACTGGGCTGTACATCTGGCACTACCCAACTGGGTCCAAACAAAACAG GTCAGGACCCCGTGGTCTAATAGTGGGACTAAGTCTCTGCCCCGGTACTCTCTCCAGATT TCAGGCTCCCTGCTTGAGGCAAGGTGCCCTCACCTCTCAGGGGTACAGCCAGGATGAGGC AGAATATACTGTGTTCTATGGTACAGCAACCGCTGGTGTCTGGTGGAGGAACCAACTGACTG</p> <p>TCCTA</p>
324.	MCSP-C8 HL x l2C HL	artificial	nt	<p>TCCTA</p> <p>QVQLVQSGAEVKRPGASMKVSKASGYFTFTNYIHWVRQAPGGGLEWMGWINPNSGATNYAQKFQ GRVTMTTRDTSTVYMELSSLRSEDTAVYYCAKSWSFASWGQGTlVTVSSGGSGGGSGGGG GSDIVMTQSPDSLAVSLGERATINCKSSQSVLNSKNNRNYLAWYQQKPGQPPKLLIYWASTRESG VPDRFSGSGSGTDFTLTISGLQAEDVAVYCCQHYSTPFTFGTKVDIKSGGGSEVQLVESGG GLVQPGSLKLSCAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYADSVKDRFTISR DDSKNTAYIQMNNLKTEDAVYYCVRHGNEGNSYISYMAVWGQTLVTVSSGGSGGGSGGGG SQTVTQEP SLTVSPGGTVTLTCSGSTGAVTSGNYPNWQQKPGQAPRGLIGGTFKFLAPGTPARF SGSLIGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGKILTVL</p> <p>CAGGTCCAGCTGGTCCAGTCTGGGCTGAGGTGAAGAGGCTGGGCTCAATGAAGGTCTCCTG CAAGGCTTCTGGGTACACCTTCACCAACTACTATATACACTGGGTGCGACAGGCCCTGGACAAG GTCTTGAAGTGGATGGGTGGATCAACCCCTAACAGTGGTGCACAAACTATGCACAGAAGTTCCAG GGCAGAGTCACCATGACCAGGACACGTCACAGCAGTCTACATGGAGCTGAGCAGCCTGAG ATCTGAGGACACGGCCGTGTTACTGTGCGAAATCTGGGTCTCTGGGTCTCTGGGTGGTGGT AAGAACCTTGGTCAACGCTCTCTCAGGTGGTGGTCTGGGCGAGAGGCCAC GGTTCGACATCGTGATGACCCAGTCTCCAGCTCCCTGGCTGTGTCTCTGGCGAGAGGCCAC CATCAACTGCAAGTCCAGCCAGAGTGTTTAAACAGCAGACAAATAGGAACACTAGCTTGGT ACGACAGAAACCAGGACAGCTCTTAAGTCTCTTACTGGGCTCTACCCGGAATCCGGG GTCCCTGACCGATTGAGTGGCAGCGGTCTGGGACAGATTCTACCTCAGTGGCTGCA GGCTGAAGATGTGGCAGTTTATTCTGTGACCAACATTAAGTACTCCATTCATTTGGCCCTG GGACCAAGTGGATATCAAAATCCGAGGTGGTGGATCCAGGTGAGCTGTGGATTCACCTTCAATAA GGATTGGTGCAGCTGGAGGTGCTTGAACCTCTCATGTGCGAGCTGTGGATTCACCTTCAATAA GTACGCCATGAAGTGGTCCGCCAGCTCCAGGAAAGGTTTGAATGGTGTGTCGCATTAAGAA GTAATATAATAATATGCAACATATATGCGGATTGAGTGAAGGAGAGGTTCAACATCTCCAGA GATGATTCAAAAACACTGCCTATCTACAAATGAACACTGAAAACTGAGGACACTGCCGTGTA CTACTGTGACACATGGAACTTCGGTAATAGCTACATATCTTACTGGGCTTACTGGGCGCAAG GGACTGTGTCACCGTCTCTCAGGTGGTGGTGTCTGGCGGCGGCTCCGGTGGTGGTGGT TCTCAGACTGTGTGACTCAGGAACCTTCACACCCGTAACCTGGTGGACAGTCAACACTCAC TTGTGGCTCCTCGACTGGGCTGTACATCTGGCACTACCCAACTGGGTCCAAACAAAACAG GTCAGGACCCCGTGGTCTAATAGTGGGACTAAGTCTCTGCCCCGGTACTCTCTCCAGATT TCAGGCTCCCTGCTTGAGGCAAGGTGCCCTCACCTCTCAGGGGTACAGCCAGGATGAGGC AGAATATACTGTGTTCTATGGTACAGCAACCGCTGGTGTCTGGTGGAGGAACCAACTGACTG</p> <p>TCCTA</p>
325.	MCSP-B8 HL x l2C HL	artificial	aa	<p>TCCTA</p> <p>QVQLVQSGAEVKRPGASMKVSKASGYFTFTNYIHWVRQAPGGGLEWMGWINPNSGATNYAQKFQ GRVTMTTRDTSTVYMELSSLRSEDTAVYYCAKSWSFASWGQGTlVTVSSGGSGGGSGGGG GSDIVMTQSPDSLAVSLGERATINCKSSQSVLNSKNNRNYLAWYQQKPGQPPKLLIYWASTRESG VPDRFSGSGSGTDFTLTIDSLQPEDSATYYCQHYSTPFTFGQGTTRLEIKSGGGSEVQLVESGG</p>

326.	MCSP-B8 HL x l2C HL	artificial	nt	<p>GLVQPGGSLKLSAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNKLTEDTAVYYCVRHGNEFNSYISYWAYWGQGLVTVSSGGSGGGSGGGG SQTVVTQEPSLTVSPGGTVTLTSGSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTPARF SCSLLGGKAAITLSGVQPEDEAEYYCVLWYSNRWVFGGTTKLTIVL</p> <p>CAGGTGAGCTGGTCCAGTCTGGGCTGAGGTGAAGAGGCTCGGGCTCAATGAAGGTCTCCTG CAAGGCTTCTGGGTACACCTTCACCAACTACTATATACATGCGTGCACAGGCCCTGGACAAG GTCTTGAGTGGATGGGTGGATCAACCCCTAACAGTGTGCACAACTATGCACAGAAGTTCAG GGCAGAGTCACCATGACAGGACACGTCACAGGACAGTCCACAGGACAGTCCATGGAGCTGAGCAGCCTGAG ATCTGAGGACACGGCCGTGATTACTGTGCGAAATCCTGGGTCTCCTGGTTGCTTCTGGGTC AAGAACCTTGGTCAACGCTCTCCTCAGGTGGTGGTCTGGGGCGGGCTCCGGTGGTGGT GGTCTGACATCGTGATGACCCAGTCTCCAGACTCCCTGACTGTCTCCGGGCGAGAGGGCCAC CATCACTGCAAGTCCAGCAGAGTGTTTAACAGAAAGAACATAGGAACACTACTTAGCTTGGT ACCAGCAAAACAGGACAGCCTCTTAAGTCTCACTTACTGGGCATCTACCCGGGAATCCGGG GTCCCTGACCGATTGAGTGGCAGGGGTCTGGGACAGATTCACTCTCACCATCGATTCCCTGCA GCCTGAAGATAGTCAACTTATTACTGTGACCAACATTATAGTACTCCATTCACTTTGGCCAGG GGACCAGACTGGAGATCAAAATCCGAGGTGGTGGATCCGAGGTGAGTGGTGGTGGTGGTGGTGGT GGATTGGTGCAGCCTGGAGGTCAATTGAACTCTCATGTGAGCCTCTGGATTCACTTCAATAA GTACGCCATGAACCTGGGTCCGCGAGCTCCAGGAAAGGTTTGAATGGGTGCTCGCATAGA GTAATATAATAATTATGCAACATATTATGCCGATTGAGTGAAGAGAGGTTTCACTTCCAGA GATGATTCAAAAACACTGCCTATCTACAAATGAACAATTGAAAACTGAGGACACTGCCGTGTA CTACTGTGAGACATGGGAACCTTCGGTAATAGTACATATCTTACTGGCTTACTGGGCGCAAG GGACTCTGGTCAACGCTCTCCTCAGGTGGTGGTGGTCTGGGCGGGCGGCTCCGGTGGTGGTGGT TCTCAGACTGTGTGACTCAGGAACCTTCACTCACCGTATCACCTGGTGAACAGTCACACTCAC TTGTGGCTCCTCGACTGGGCTGTACATCTGGCAACTACCAAACTGGGTCCAAACAAACCCAG GTCAGGCAACCCGCTGGTCTAATAGTGGGACTAAGTTCTCGCCCGGCTACTCTGCCAGATTCT TCAGGCTCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGC AGAATATTACTGTGTTCTATGGTACAGCAACCCGCTGGGTGCTGGGTGAGGAAACCAACTGACTG TCCTA</p>
327.	MCSP-B7 HL x l2C HL	artificial	aa	<p>QVQLVQSGAEVVRPGASMKVSKASGYFTFTNYIHWVRQAPGQGLEWMGWINPNSGATNYAQKFQ GRVTMTTRDSTSTVYMEISLRSEDTAVYYCAKSWVFWFASWGQGLVTVSSGGSGGGSGGGG GSDIVMTQSPDLSLVSLGERTTINCKSSQSVLNSKNRNYLAWYQKPGQPPKLLIYWASTRESG VPDREFSGSGSDFTLTIDSLQPEDIAITYCQQHYSTPFTFGQTRLEIKSGGGSEVQLVESGG GLVQPGGSLKLSAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNKLTEDTAVYYCVRHGNEFNSYISYWAYWGQGLVTVSSGGSGGGSGGGG SQTVVTQEPSLTVSPGGTVTLTSGSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTPARF SCSLLGGKAAITLSGVQPEDEAEYYCVLWYSNRWVFGGTTKLTIVL</p>
328.	MCSP-B7 HL x l2C	artificial	nt	<p>CAGGTGAGCTGGTCCAGTCTGGGCTGAGGTGAAGAGGCTCGGGCTCAATGAAGGTCTCCTG</p>

HL				CAAGGCTTCTGGGTACACCTTCAACCAACTACTATATACACTGGGTGGACAGGCCCTGGACAAG GTCTTGAGTGGATGGGTGGATCAACCTTAAACAGTGGTGCACAAACTATGCACAGAAGTTCAG GGCAGAGTCACCATGACACAGGACAGTCCACGAGCAGCTACATGAGAGCTGAGCAGACCTGAG ATCTGAGGACACGGCCGTGTATTACTGTGCGAAATCCTGGGTCTCCTGGTTTCTTCTGGGGT AAGGAACCTTGGTACCGTCTCCTCAGGTGGTGGTCTGGCGGGCGGGCTCCGGTGGTGGT GGTCTGACATCGTATGACCCAGTCTCCAGACTCCCTGACTGTCTCTGGCGAGAGACCAC CATCAACTGCAAGTCCAGCCAGAGTGTCTTAAACAGCAAGAAATAGGAATCTAGCTTGGT ACCAGCAGAAACAGGACAGCTCTTAAGTCTCACTTACTGGGCATCTACCCGGGAATCCGGG GTCCCTGACCGATTAGTGGCAGCGGTCTGGGACAGATTTCATCTCACCATCGATTCCCTGCA GCCTGAAGATATTGCAACTTATTACTGTACGCAACATATAGTACTCATTCATCTTGGCCAGG GGACCAGACTGGAGATCAAAATCCGGAGGTGGTGGATCCGAGGTGAGCTGGTCGAGCTCTGGAGGA GGATTGGTGAGCCTGGAGGTCTTGAACCTCTCATGTGAGCCTCTGGATTCACTTCACTTCAATAA GTACGCCATGAATGGGTCCGCCAGGTCCAGGAAGGTTTGAATGGTTGCTCGCATAAAGAA GTAATATAATAATTATGCAACATATTATGCCGATTTCAGTGAAGACAGGTTTACCATCTCCAGA GATGATTCAAAAACACTGCCCTATCTACAAATGAACAACTTGAACAACTGAGGACACTGCCGTGTA CTACTGTGAGACATGGGAACCTTCGGTAATAGTACATATCTACTTGGCTTACTGGGGCCAAAG GGACTCTGGTCAACCTCTCCTCAGGTGGTGGTGTCTGGCGGGCGGGCTCCGGTGGTGGTGGT TCTCAGACTGTGTGACTCAGGAACCTTCACTCACCCTATCACCCTGGTGGACAGTCACTCAC TTCTGGCTCTCCACTCGCCCTGTTACATCTGCCAACTACCCAACTCGCTCCAAACAAACACAG GTCAGGCACCCCGTGTCTAATAGGTGGGACTAAGTTCCTCGCCCCGGTACTCTCTGCCAGATT TCAGGCTCCCTGCTTGAGGCAAGGTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGC AGAATATTACTGTCTTATGTTACAGCAACCGCTGGGTCTTCGGTGGAGGAACCAACTCACTG TCCTA	
329.	MCSP-G8 HL x I2C HL	aa	artificial	artificial	nt
330.	MCSP-G8 HL x I2C HL	nt	artificial	artificial	nt

<p>GGTTCTGACATCGTGATGACCCAGTCTCCAGACTCCCTGACTGTGTCTCTGGGCGAGAGGGCCAC CATCAACTGCAAGTCCAGCCAGAGTGTCTTAAACAGCAAGAAATAAGGAACACTATTAGCTTGGT ACCAGAGAAACAGGACAGCTCTTAAGCTGCTCACTTACTGGGATCTACCCGGGAATCCGGG GTCCCTGACCGATTGAGTGGAGCGGTCTGGGACAGATTCACTCTCACCATCGATTCCCTGCA GCCTGAAGATAGTCAACTTATTACTGTCAAGCAACATTATAGTACTCACTTCTGGCCAGG GGACCAGACTGGAGATCAAAATCCGAGGTGGTGGATCCGAGGTGAGCTGTCGAGTCTGGAGGA GGATTGGTGCAGCTGGAGGTCAATTGAACTCTCATGTGAGCTCTGATTCACCTTCAATAA GTACGCCATGAACCTGGTCCGCCAGGTCCAGGAAAGGTTTGAATGGTGTCTCGCATAGAA GATGATCAAAAACACTGCCTATCTACAAATGAACAACCTGAAAACCTGAGGACACTGCCGTGTA CTACTGTGTGACATGGAACTTCGGTAATAGTACATATCTACTGGGCTTACTGGGCGCAAG GGACTGTGTCAACCTCTCCTCAGGTGGTGGTCTGGGCGCGGGCTCCGGTGGTGGTGGT TCTCAGACTGTGTGACTCAGGAACCTTCACTCACCCTATCCTGGTGGACAGTCACTCAC TTGTGGTCTCTGACTGGGCTGTACATCTGGCACTACCAAACTGGTCCAAACAAACCCAG GTCAGGCAACCCCTGGTCTAATAGTGGGACTAAGTTCCTCGCCCCGCTACTCCTGCCAGATT TCAGGCTCCCTGCTTGAGGCAAGGTGCCCTCACCCTCTCAGGGGTACAGCCAGAGGATGAGG AGAAATATTACTGTGTCTATGTTACAGCAACCGCTGGGTCTGGTGGAGGAACCAAACTGACTG TCCTA</p>		<p>QVQLVSGAEVKRPGASMKVSCKASGYFTTNYIHWVQAPEGQLEWMGWINPNSGATNYAQKFO GRVTMRDTSSTVYMESSLRSEDYAVYCAKSWVSWFASWQGLTVTVSSGGSGSGSGSGG GSDIVMTQSPDSLAVSLGERATINCKSSQSVLNSKNRNLYAWYQKPGQPKLLIYWASTRESG VPDRFSGSGSTDFTLTIDSLQAEKDSATYYCQQHYSTPTFGQTRLEIKSGGGSEVQLVESGG GLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNLIKTEDTAVYYCVRIHGFNSYISYWAYWGQGLTVTVSSGGSGSGSGSGGG SQFVVTQEPSTLTVSPGGTVTLTLCGSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTPARF SGSLLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGKLTIVL</p>
<p>331. HL</p>	<p>MCSP-D5 HL x I2C HL</p>	<p>aa artificial nt</p>
	<p>332. HL</p>	<p>MCSP-D5 HL x I2C HL</p>

<p>GGACCAGACTGGAGATCAAAATCCGGAGGTGGTGGATCCGAGGTGCGAGTGGTGGAGTCTGGAGGA GGATTGGTGCAGCTGGAGGTGATTGAAACTCTCATGTGCAGCTCTGGATTACCTTCAATAA GTACGCCATGAACGTGGTCCGCCAGGTCCAGGAAAGGTTTGAATGGTTGTCGCATAAGAA GTAATATAATAATATGAACATATATGCCGATTCAAGTGAAGACAGGTTACCATCTCCAGA GATGATCAAAAAACACTGCCATCTACAAATGAACAACCTGAAACACTGAGGACACTGCCGTGA CTACTGTGAGACATGGAACTTCGGTAATAGCTACATACTACTGGGCTTACTGGGGCCAAG GGACTCTGTCACCGTCTCTCAGGTGGTGGTCTGGGGGGGGGGTCTCGGTGGTGGTGGT TCTCAGACTGTGTGACTCAGGAACCTTCACTCACCCTATACCTGGTGGACAGTACACTCAC TTGTGGTCTCTGACTGGGCTGTACATCTGGCACTACCAAACTGGTCCAAACAAACAG GTCAGGCACCCCGTGGTCAATAGGTGGACTAAGTCTCTCGCCCCGGTACTCTGCCAGATT TCAGGTCCTCTGTTGGAGGCAAGGTGCCCTCACCCTCAGGGGTACAGCCAGAGGATGAGG AGAATATTACTGTCTTATGGTACAGCAACCGCTGGTGTGGTGGAGGAACCAACTGACTG TCCTA</p>	<p>QVQLVQSGAEVKRPGASMKVSKASGYTFNYYIHWRQAPQGLEWMGWINPNSGATNYAQRFQ GRVTMTRTSTVYMELSLRSEDTAVYCAKSWFASWQGTILTVSSGGSGSGSGSGG GSDIVMTQSPDSLAVSLGERATINCKSSQSVLNKNNNYLAWYQQKPKLLIYWASTRESG VPDRFSGSGSTDFTLTIDVLQPEDIAITYCQQHYSTPTTFGQGTTRLEIKSGGGGSEVQLVESGG GLVQPGGSLKLSKAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNLLKTEDTAVYYCVRHGNFNSYISYWAYWGQTLTVSSGGSGSGSGSGGG SQTIVTQEPSTLVSPGGTVTLTCSSTGAVTSGNYPNWVQKPGQAPRGLIGSTKFLAPGTPARF SGSLGKGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGKLTIVL</p>	<p>CAGTGGAGCTGGTCCAGTCTGGGCTGAGGTGAAGGCTGGGCTCAATGAAGTCTCCTG CAAGGCTCTGGGTACACTTCAACCACTACTATATACACTGGGTGCGACAGGCCCTGGACAAG GTCTTGAGTGGATGGTTGGATCAACCCCTAACAGTGGTGGCCACAACTATGCACAGAAGTCCAG GGCAGAGTCACCATGACCAGGGACACGTCCACGACGACAGTCTACATGGAGCTGAGCAGCCTGAG ATCTGAGGACACGGCCGTGATTACTGTGCGAAATCCTGGTCTCCTGGTTTGTCTCCTGGGTC AAGGAACCTGGTCAACGTCTCCTCAGGTGGTGGTGGTGGGCGGGGCTCCGGTGGTGGT GGTCTGACATCGTGATGACCCAGTCTCCAGACTCCCTGGCTGTCTCTGGCGAGAGGGCCAC CATCACTGCAAGTCCAGCCAGAGTGTTTAAACAGCAAGAAATAGGAACATACTAGCTTGGT ACCAGCAAAACCCAGGACAGCCTCCTAAGTGTCTTACTGGGCATCTACCCGGGAATCCGGG GTCCCTGACCGATTGAGTGGCAGCGGTCTGGGACAGATTCACTCTCACCATCGATGTCTCTGCA GCCTGAAGATATTGCAACTTATTACTGTGACCAACATTATAGTACTCACTTCTTGGCCAGG GGACCAGACTGGAGATCAAAATCCGGAGGTGGTGGATCCGAGGTGAGTGGTGGTGGTGGGGA GGATTGGTGCAGCCTGGAGGTGATTGAAACTCTCATGTGAGGCTTGGATTCACTTCAATAA GTACGCCATGAACGTGGGTCCGCCAGGCTCCAGGAAAGGTTTGAATGGTGGTGGTGGTGGTGGT GTAATATAATAATATGCAACATATTATGCCGATTGAGTGAAGACAGGTTTACCATCTCCAGA GATGATTCAAAAAACACTGCCTATCTACAAATGAACAACCTGAAACTGAGGACACTGCCGTGTA</p>
<p>333.</p>	<p>MCSP-F7 HL x I2C HL</p>	<p>aa</p>
	<p>artificial</p>	<p>nt</p>
	<p>MCSP-F7 HL x I2C HL</p>	<p>artificial</p>
<p>334.</p>	<p>MCSP-F7 HL x I2C HL</p>	

				<p>CTACTGTGTGAGACATGGGAACTTCGGTAATAGCTACATATCCTACTGGGCTTACTGGGCCAAG GGACTCTGGTCACCGTCTCCTCAGGTGGTGGTGGTCTGGGGGGGGGGTCTGGTGGTGGTGGT TCTCAGACTGTGTGACTCAGGAACCTTCACTCACCCTACCTGGTGGAACTCAGTACACTCAC TTGTGGTCTCTGACTGGGCTGTACATCTGGCAACTACCAAACTGGTCCAAACAAACAG GTCAGGCACCCCGTGGTCTAATAGTGGGACTAAGTCTCGCCCCCGTACTCTCCAGATTCTC TCAGGCTCCCTGCTTGAGGCAAGGTGCCCTCACCCTCCTCAGGGGTACAGCCAGGATGAGGC AGAATATTACTGTGTCTATGTACAGCAACCGTGGTGTGGTGGAGAACCAACTGACTG TCCTA</p>
335.	MCSP-G5 HL x l2C HL	artificial	aa	<p>QVQLVQSGAEVKRPGASMKVSKASGYTFNYYIHWVRQAPGGLEWMGWINPNSGATNYAQKFQ GRVTMRDSTSTVYMELSSLRSEDYVYCAKSWSFASWGQDTLVTVSSGGGGGGGGGG GSDIVMTQSPDSLAVSLGDRATINCKSSQSVLNSKNNRNYLAWYQQKPGQPPKLLIYWASTRESG VPDRFSGSGSTDFLTIDSLQPEDSATYQCQHYSTFTFGQGRLEIKSGGGGSEVQLVESGG GLVQPGGSLKLSAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNLLKTEDAVYYCVRHGFNSYI SYWAYWGQDTLVTVSSGGGGGGGGGGGG SQTIVTQEPSTLTVSPGGTTLTCSGSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTPARF SGSLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGKLTIVL</p>
336.	MCSP-G5 HL x l2C HL	artificial	nt	<p>CAGTGCAGCTGGTCCAGTCTGGGCTGAGGTGAAGCGCTGGGGCTCAATGAAGGTCTCCTG CAAGGCTCTGGGTACACCTTCAACCACTACTATATACACTGGTGCACAGGCCCTTGACAAG GTCTTGAAGTGGATGGGTGGATCAACCTAACAGTGTGGCACAACATATGCACAGAAGTTCAG GGCAGATCACCATGACCAGGGACACGTCCACGAGCACAGTACATGGAGCTGACGAGCCTGAG ATCTGAGGACACGGCCGTGTATTACTGTGCGAAATCCTGGGTCTCTGGTTTGTCTCTGGGGTC AAGGAACCTTGGTCACCGTCTCCTCAGGTGGTGGTGTCTGGCGGGCGGGTCCGGTGGTGGT GGTCTGACATCGTGATGACCCAGTCTCCAGACTCCCTGGCTGTCTCTGGCGACAGGGCCAC CATCACTGCAAGTCCAGCCAGAGTGTTTAAACAGCAAGAACAAATAGGAACACTTAGCTTGGT ACCAGCAAAACCCAGCACAGCCTCCTAAGTGTCTCAITTAAGGCACTACCCGGGAATCCGGG GTCCTGACCGATTGAGTGGCAGCGGTCTGGGACAGATTCACTCTCACCATCGATTCCCTGCA GCCTGAGGATAGTGCAACTTATTACTGTGCAACAAATTATAGTCTCACTTTCCTGGCCAGG GGACCAGACTGGAGATCAATCCGGAGGTGGTGGATCCGAGGTGCAGTGGTCGAGTCTGGAGGA GGATTGGTGCAGCCTGGAGGTGATTGAACTCTCATGTGCGACCTCTGGATTCACTTCAATAA GTACGCCATGAACCTGGTCCGCCAGGTCCAGGAAAGGTTTGAATGGGTGCTCGCATAGA GTAATATAATAATTATGCAACATATTATGCCGATTGAGTGAAGACAGGTTACCATCTCCAGA GATGATTCAAAAAACACTGCCTATCTACAAATGAACAACTTCAAACTGAGGACACTGCCGTGTA CTACTGTGTGAGACATGGGAACTTCGGTAATAGCTACATACTACTGGGCTTACTGGGGCCAAAG GGACTCTGGTCACCGTCTCCTCAGGTGGTGGTGGTCTGGCGGGGGGGTCCGGTGGTGGTGGT TCTCAGACTGTGTGACTCAGGAACCTTCACTCACCCTATCACTGGTGAACAGTACACTCAC TTGTGGCTCCTCGACTGGGGTGTACATCTGGCAACTACCAAACTGGGTCCAAACAAACAG GTCAGGCACCCCGTGGTCTAATAGTGGGACTAAGTTCCTCGCCCCCGGTACTCTGCCAGATTCTC</p>

5
10
15
20
25
30
35
40
45
50
55

55	340.	MCSP-G10 HL x I2C HL	artificial	nt	<p>GSDIVMTQSPDSLAVSLGERATINCKSSQSVLSSNNKNYLNWYQKPGQPPLLIYWASTRESG VPDRFSGSGSDFTLTITSSLOAEDVAVYQCQHGHTPPFAFGQGTKLEIKSGGGSEVQLVESGG GLVQPGGSLKLSAASGFTFNKYAMNWRQAPCKGLEWVARIRSKYNNIATYYADSVKDRFTISR DDSKNTAYLQMNLIKTEDTAVYCVRHGNEGNSYISYWAYWGQTLTVTVSSGGSGSGSGSGGG SQTVVTQEPSTLTVSPGGTVTLTCGSSTGAVTSNYPNWPQKPGQAPRGLIGGCTKFLAPGTPARF SGSLGGKAALTLSGVQPEDEAEYCYVLWYSNRWVFGGKLTIVL</p> <p>CAGGTGCAGCTGGTCCAGTCTGGGGCTGAGCTGAAGAGCGCTGGGGCTCAATGAAGGTCTCCTG CAAGGCTTCTGGGTACACCTTCACCACTACTATATACACTGGGTGCACAGGCCCTTGACAAG GTCTTGAGTGGATGGTTGGATCAACCTTAACAGTGGTGCCACAACTATGCACAGAAGTCCAG GGCAGAGTCAACATGACCAGGACACGTCCACGAGCACAGTCTACATGGAGCTGACAGCTGAG ATCTGAGGACACGGCCGTGTATTACTGTGCGAAATCCTGGGTCTCCTGGTTTGTCTTCTGGGTG AAGGAACCTTGGTCAACGCTCTCCTCAGGTGGTGGTCTTCTGGCGGGCGGCTCCGGTGGTGGT GGTCTGACATCGTGAIGACACAGTCTCCAGACTCCCTGGTGTGTCTCTGGCGGAGAGGCCAC CATCAACTGCAAGTCCAGCCAGAGTGTCTATCCAGCTCCAACAATAAGAACTACTTAAATTGGT ACCAGAGAAACCCAGGACAGCCTCCTAAGTTGCTCATTTACTGGGCACTACCCGGGAATCCGGG GTCCCTGACCGATTGAGTGGCAGCGGTCTGGACAGATTTCACTCTCAACATCAGCAGCTGCA GGCTGAAGATGTGGCGGTTTATTACTGTCAACAACATTTAATACTCGTTGCTTGGCCAGG GGACCAAGCTGGAGATCAAAATCCGGAGGTGGTGGATCCGAGGTGAGCTGGTGGAGTCTGGAGGA GGATTGGTGACGCTGGAGGTCATTGAACCTCTCATGTGCAGCCTCTGGATTCACCTTCAATAA GTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGGTTTGAATGGTTGCTCGCATAGAA GTAATATAATAATTAIGCAACATATTATGCGGATTGAGTGAAGACAGGTTTCAACATCTCCAGA GATGATTCAAAACACACTGCCATCTACAAATGAACAACCTTGAACACTGAGGACACTGCCGTGTA CTACTGTGTGAGACATGGGAACCTTCGGTAAATAGTACATATCTACTGGGCTTACTGGGGCCAAAG GGACTGTGTCAACCGTCTCCTCAGGTGGTGGTGGTCTGGCGGGCGGGCTCCGGTGGTGGTGGT TCTCAGACTGTGTGACTCAGGAACCTTCACTACCGGTATCACCTGGTGAACAGTCACTCAC TTGTGGCTCCTCGACTGGGCTGTACATCTGGCAACTACCAAACTGGGTCCAACAAAAACCCAG GTCAGGCACCCCGTGGTCTAATAGGTGGGACTAAGTTCCTCGCCCCGGTACTCCTGCGCAGATT TCAGGCTCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGC AGAAATATTACTGTGTCTTATGGTACAGCAACCGCTGGGTGTTCGGTGGAGGAACCAACTGACTG TCCTA</p>
50	341.	Human CD3 ϵ 1-8 (N-terminus)	human	aa	QDGNEEMG
45	342.	<i>Saimiri sciureus</i> CD3 ϵ 1-8 (N-terminus)	<i>Saimiri sciureus</i>	aa	QDGNEEIG
40	343.	Thioate-modified CpG-Oligonucleotide	artificial	nt	TCCATGACGTTCTCTGATGCT

344.	MVH1		artificial	nt	(GC)AGGTGCAGCTCGAGGAGTCAGGACCT
345.	MVH2		artificial	nt	GAGTCCAGCTCGAGCAGTCTGGACCT
346.	MVH3		artificial	nt	CAGTCCAACTCGAGCAGCTGGGGCT
347.	MVH4		artificial	nt	GAGTTCAGCTCGAGCAGTCTGGGGCA
348.	MVH5		artificial	nt	GA (AG) GTGAAGCTCGAGGAGTCTGGAGGA
349.	MVH6		artificial	nt	GAGTGAAGCTTCTCGAGTCTGGAGGT
350.	MVH7		artificial	nt	GAAGTGAAGCTCGAGGAGTCTGGGGGA
351.	MVH8		artificial	nt	GAGTTCAGCTCGAGCAGTCTGGAGCT
352.	MuVHBstEII		artificial	nt	TGAGGAGACGGTGACCGTGGTCCCTTGGCCCCAG
353.	MUVK1		artificial	nt	CCAGTCCGAGCTCGTTGTGACTCAGGAATCT
354.	MUVK2		artificial	nt	CCAGTCCGAGCTCGTTGTGACGCAGCCGCC
355.	MUVK3		artificial	nt	CCAGTCCGAGCTCGTGTCTCACCCAGTCTCCA
356.	MUVK4		artificial	nt	CCAGTCCGAGCTCCAGATGACCCAGTCTCCA
357.	MUVK5		artificial	nt	CCAGATGTGAGCTCGTGTATGACCCAGACTCCA
358.	MUVK6		artificial	nt	CCAGATGTGAGCTCGTGTATGACCCAGTCTCCA
359.	MUVK7		artificial	nt	CCAGTCCGAGCTCGTGTATGACACAGTCTCCA
360.	MuVhIndIII/BsW1		artificial	nt	TGGTGCACTAGTGTACGTTTGATCTCAAGCTGGTCCC
361.	forward primer		artificial	nt	GATCTGGTCTACACCATCGAGC
362.	reverse primer		artificial	nt	GGAGCTGTCTGGCTCAGTGAGG
363.	forward primer		artificial	nt	TCCAGCTGAGCATGTCTGATGG
364.	reverse primer		artificial	nt	CGATCAGCATCTGGGCCCCAGG
365.	forward primer		artificial	nt	GTGGAGCAGTTCACTCAGCAGGACC
366.	reverse primer		artificial	nt	GCCTTCACACCCAGTACTGGCC
367.	forward primer		artificial	nt	TCCCGTACGAGATCTGGATCCCAATTGGATGCGGACTCGTGTCTCACACAGAGG
368.	reverse primer		artificial	nt	AGTGGTTCGACTCACACCCAGTACTGGCCATTCTTAAGGGCAGGG
369.	forward primer		artificial	nt	GAGGAATTACCAATGCCGCTGCTGCTACTGCTCCCCCTGCTGTGGGCAGGGGCCCTGGTATGG
370.	reverse primer		artificial	nt	GATTGTAACTGTATTGGTACTTCC
371.	forward primer		artificial	nt	ATTCCGCTCTCTGGGGATCC
372.	reverse primer		artificial	nt	GCATAGGAGACATTGAGCTGGATGG
373.	forward primer		artificial	nt	GCACCAACCTGACCTGTCCAGG
374.	reverse primer		artificial	nt	AGTGGTTCGACTCACTGGGTCCGAGCCTCTGAGTATTCCG
375.	forward primer		artificial	nt	CACTGTGGCCCAAGTTCCAGG
376.	reverse primer		artificial	nt	GACATACCACACAAATTCATACGG
377.	forward primer		artificial	nt	GCTCTGCTCGCGCCGAGATGTGG
378.	reverse primer		artificial	nt	ACGCTGGACACCACTCCAGG

379.	forward primer		nt	GGTCTACTGAGTGGCAGAGG
380.	reverse primer	artificial	nt	ACTTGTGTGGCTGCTTGGAGC
381.	forward primer	artificial	nt	GGTGAAGTCTATCCAGATGG
382.	reverse primer	artificial	nt	GTGCTCTGCCTGAAGCAATTCC
383.	forward primer	artificial	nt	CTCGGCTTCCCTCTTCGGGTGG
384.	reverse primer	artificial	nt	GCATATTCAATTGCTGGGTAACTGG
385.	macaque PSMA (Cynomolgus)	artificial	nt	ATGTGGAATCTCTGACGAAACCCGACTCGGTGTGGCCACCGCGCGCCGCGTGGCTGTG CGCTGGGGCACTGGTGTCTGGCGGTGGCTTCTTCTCTCGGCTTCTTCTCGGATGTTTATAA AATCCTCCAGTGAAGCTACTAACATTACTCCAAAGCATAATATGAAGCATTTTGGATGAACG AAAGCTGAGAACATCAAGAGTTCTTACATAATTTACACAGATACCACATTTAGCAGGAACAGA ACAAACTTTCAACTTGCAAAGCAATTCATCCAGTGAAAGAAATTTGGCCTGGATTCTGTG AGTAACTCATATATGATGTCCCTGCTTACCCAAATAAGACTCATCCCACTACATCTCAATA ATTAATGAAGATGGAATGAGATTTCAACACATCATATTATTTGAACCACTCTCTGCAGATATGA AAATGTTTCGGATATTGTACCCACTTTCAGTGTCTCTCTCAAGGAATGCCAGAGGGGATC TAGTGTATGTTAACTATGCACGAACTGAAGACTTCTTAAATTTGGAACGGGACATGAAATCAAT TGCTCTGGGAAATTTGTAATGCCAGATATGGGAAAGTTTTCAGAGGAAATAGGTTAAAAATGC CCAGCTGGCAGGGGCCACAGGAGTCAATTCCTACCTCAGACCTTCTGACTACTTTCCTCTGGG TAAAGTCTTATCCAGATGGTTGGAATCTCTCGAGGTGGTGTCCAGCGTGGAATATCTCTAAAT CTGAATGGTGCAGGAGACCTCTCAACAGGTTACCCAGCAATGAATATGCTTATAGGCTGG AATGGCAGAGGCTGTGGTCTTCCAAAGTATCCCGTTTATCCATTTGGTACTATGATGCACAGA AGCTCTAGAAAAAATGGTGGCTCAGCATCACAGATAGCAGTGGAGAGGAAGTCTCAAGTG CCTACAATGTTGGACCTGGCTTACTGGAACTTTTCTACAAAAAGTCAAGATGCATCCCA CTCACAGTGAAGTGACAGAATTTACAATGTGATAGGTACTCTCAGAGGAGCAGTGGAAACCAG ACAGATACGTCAATCTGGGAGGTCAACGGGACTCATGGGTGTTTGGTGGTATTGACCTCAGAGT GGAGCAGCTGTTGTTTCATGAAATGTGAGGAGCTTTGGAACGCTGAAAAAGGAGGTGGAGACC TAGAAGAACAAATTTGTTTGAAGCTGGGATGCAGAAAGAAATTTGGTCTTCTTGGTCTACTGAAT GGGCAGAGGAGAAATCAAGACTCCTTCAAGAGCTGGCTGGCTTATATTAATGCTGATCTGCT ATAGAGGGAAACTACACTCTGAGAGTTGATTGTACACCACTGATGTACAGCTTGGTATACAACCT AACAAAAGAGCTGGAAGCCCTGATGAAGCTTGAAGGCAAACTCTCTTATGAAGTTGGACTA AAAAAAGTCTTCCCCGAGTTCAGTGGCATGCCAGGATAAGCAAAATTTGGATCTGGAATGAT TTTGAGGTGTTCTTCCACGACTTGAATTCCTCAGGAGAGCAGGTATCTACTAAAAATTTGGGA AACAAACAAATTCAGCAGCTATCCACTGTATCAGATGTCTATGAGACATATGAGTTGGTGAAA AGTTTATGATCCAAATTTAAATATCACCTACTGTGGCCAGGTTTCAGGAGGGATGGTCTTT GAACTAGCCAAATTCGCTAGTGTCTCTTGTATGTCGAGATTTATGCTGTAGTTTAAAGAACTA TGCTGACAAAAATCTACAATAATTTCTATGAACATCCACAGGAAATGAAGACATACAGTGTATCAT TTGATTCACTTTTTTCTGCAGTAAAGAAATTTTACAGAAATTTCTTCCAGTTTCAGCGAGAGACTC CGGACTTTGACAAAAAGCAACCAATATTATTAAGAATGATGAATGATCACTCATGTTCTTCTGGA

					<p>AAGCATTTATTGATCCATTAGGGTTACCAGACAGACCTTTTATAGGCATGTCTATGCTC CAAGCAGCAACAAGATATGAGGGGAGTCATCCAGGAATTTATGATGCTCTGTTGATATC GAAAGCAAGTGGACCTTCCCAGGCTGGGAGAGAGTGAAGACAGATTCTGTTGCAACCTT CACAGTCAAGCAGCTGCAGAGACTTTGAGTGAAGTGGCCTAA</p>
386.	macaque PSMA (Cynomolgus)	artificial	aa		<p>MWLLHETDSAVATARRPRWLCAGALVLAGGFFLLGFLGWFIKSSSEATNITPKHNNKAFIDEL KAENIKKFLHNETQI PHLAGTEQNFOLAKQIQSQWKEFGDVELTHYDVLLSYPNKTHPNYSI INEDGNEIFNTSLFEPYPAGYENVSIVPPFSAFSPQGMPEGLVYVNYARTEDFFKLERDMKIN CSGKIVARIYKGVFRGNKVNAQLAGATGVILYSDPADYFAPGVKSYFDGWNLPGGGVQRGNILN LNGAGDPLTPGYPANAYARRGMAEAVGLPSIPVHPIGYDAQKLLKMGGSASPDSSWRGSLKV PYNVPGFTGNFSTQKVKMHIHSTSEVTRIYNVIGTLRGAVEPDRYVILGGHRDSWVFGGIDPQS GAAVVEIVRSFGLKKEGWRPRRTILFASWDAEEFGLLGSTEWAEENRLLQERGVAVINADSS IEGNYTLRVDCPTIMYSLVYNLTKELESPDEGEFKSLYESWTKKSPSEFSGMPRI SKLGSND FEVFFQRLGIASGRARYTKNWETNKFSSYPLYSHSVYETVELVEKFYDPMFYHLITVAQVRGGMVF ELANSVVLPPDCRDYAVVLRYADKIYINISMKHPQEMKTSVSFSLFSAVKNFTEIASKFSERL RDFDKSNPILLRMMNDQLMFLERAFIDPLGLPDRPFYRHHVYAPSSHKNKYAGESFPGIYDALFDI ESKVDPSQAWGEVKKQISVAITFTVQAAETLSEVA</p>
387.	PSMA-3 L	artificial	aa		<p>DIQMTQSPKFMSTSVGDRSVTCKASQNVDTNVAVYQQKTGQSPKALIIYSASYRSDVDFRFTGS ESGTDFTLTIISNVQSEDLAEYFCQQYDSYPTFGGTTKLEIK</p>
388.	PSMA-3 L	artificial	nt		<p>GTGATCCAGATGACCCAGTCCCCCAAGTTCAATGCCACCTCCGTGGGCGACAGAGTCCGTGAC CTGCAAGGCTCCAGAACGCTGGACACCAACCTGGCTGGTATCAGCAGAAAGCCCGGACAGTCCC CTAAGGCCCTGATCTACTCCGCCCTCCTACCGGTACTCTGACGTGCCTGACCGGTTCCCGGCTCC GAGTCCGGCACCGACTTCACCCGTGACCATCTCCAACTGAGTCTGAGGACCTGGCCGAGTACTT CTGCAGCAGTACGACTCCTACCCCTTACACCTTCGGCGGAGGACCAAGCTGGAATCAAG</p>
389.	PSMA-3 LCDR1	artificial	aa		KASQNVDTNVA
390.	PSMA-3 LCDR2	artificial	aa		SASYRYS
391.	PSMA-3 LCDR3	artificial	aa		QQYDSYPYT
392.	PSMA-3 H	artificial	aa		<p>DVKLVESGGGLVKPGESLKLSCIASGFTFSDYMYWVRQTPEKRLEWVAIISDGGYTYYSIDIK GRFTISRDNAKNNLYLQMSLSKSEDTAMYCTRGEPLLRHGAMDYWGLGTSVTVS</p>
393.	PSMA-3 H	artificial	nt		<p>CACGTGAAACTGGTGGAGTCTGGGGGGGAGTGGTGAAGCCCTGGGAGTCCCTGAAGCTCTCTG TATCGCTCCGGCTTACCTTCTCCGACTACTACATGTACTGGTGGCAGACCCCTGAGAAGC GGGTGGAATGGTGGCCATCATCTCCGACGGGGTACTACACTACTCCGACATCATCAAG GGCCGGTTCACCATCTCCCGGGACACGCCAAGAACCAACCTGTACCTGCAGATGTCTCTCCTGAA GTCCGAGGACACCGCCATGTACTACTGCACCCGGGCTTCCCTCTGCTGAGACACGGCGGCATGG ATTACTGGGGCCTGGGCACCTCTGTGACCGTGTCTCT</p>
394.	PSMA-3 HCDR1	artificial	aa		DYMY
395.	PSMA-3 HCDR2	artificial	aa		IISDGGYTYYSIDIK

396.	PSMA-3 HCDR3	artificial	aa	GFLLRHGAMDY	DVKLVESGGGLVKPGESLKLSCIASGFTFSDYMYWVRQTPEKRLIEWVAIIISDGGYTYYSYSDIIK
397.	PSMA-3 HL	artificial	aa		GRFTISRDNAKNNLYLQMSLSKSEDTAMYCTRGFPLLRHGAMDYWGLTSVTSSGGSGGGG SGGGSDIQMTQSPKFMSTSVQDRVSVTKASQNVDTNVAWYQKPGQSPKALIYSASYRYSVDP DRFTGSESGTDFTLTISNVQSEDLAEYFCQYDSYPYTFGGGKLEIK
398.	PSMA-3 HL	artificial	nt		GACGTGAACACTGGTGGAGTCTGGCGGGGACTGGTGAAGCCTGGCGAGTCCCTGAAGTGTCTCTG TATCGCCTCCGGCTTACCTTCTCCGACTACTACATGTAAGTGGTGGCGAGACCCCTGAGAAGC GGCTGGAATGGTGGCCATCATCTCCGACGGCGCTACTACCTACTCCGACATCATCAAG GGCGGTTCACCATCTCCGGGACACGCCAAGAACCACTGTACCTGCAGATGTCTCCCTGAA GTCCGAGACACCGCCATGTACTACTGACCGGGCTTCCCTCTGTGAGACACGGGCGCATGG ATTACTGGGCGCTGGCACCTCTGTGACCGTCTCTGGCGAGGGGAGTGGAGGCGGAGGA AGTGGAGGGGGGATCCGACATCCAGATGACCCAGTCCCCAAGTTATGTCCACCTCCGTGGG CGACAGAGTGTCCGTGACCTGCAAGGCTCCAGAACAGTGGACACCAACGTGGCTGGTATCAGC AGAAGCCCGCCAGTCCCTAAGGCCCTGATCTACTCCGCTCTCTACCGGTACTCTGACGTGCCT GACCGGTTACCGGCTCCGAGTCCGGCACCGACTTACCTTACCTTCCAAACGTGCAGTCTGA GGACCTGGCGGAGTACTTCTGCCAGCAGTACGACTCTACCTTACACCTTCGGCGGAGGAGCA AGCTGGAATCAAG
399.	PSMA-3 HL x I2C HL	artificial	aa		DVKLVESGGGLVKPGESLKLSCIASGFTFSDYMYWVRQTPEKRLIEWVAIIISDGGYTYYSYSDIIK GRFTISRDNAKNNLYLQMSLSKSEDTAMYCTRGFPLLRHGAMDYWGLTSVTSSGGSGGGG SGGGSDIQMTQSPKFMSTSVQDRVSVTKASQNVDTNVAWYQKPGQSPKALIYSASYRYSVDP DRFTGSESGTDFTLTISNVQSEDLAEYFCQYDSYPYTFGGGKLEIKSGGGSEVQLVESGGGL VQPGSLKLSAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGLTVTVSSGGSGGGSGGGGSGQ TVVTQEPSTLTVSPGGTVTLTCGSSTGAVTSGNYPNWWVQKPGQAPRGLIGGTFKFLAPGTPARFSG SLLGGKAALTLSGVQPEDEAEYCVLWYSNRWVFGGKLTVL
400.	PSMA-3 HL x I2C HL	artificial	nt		GACGTGAACACTGGTGGAGTCTGGCGGGGACTGGTGAAGCCTGGCGAGTCCCTGAAGTGTCTCTG TATCGCCTCCGGCTTACCTTCTCCGACTACTACATGTAAGTGGTGGCGAGACCCCTGAGAAGC GGCTGGAATGGTGGCCATCATCTCCGACGGCGCTACTACCTACTACTCCGACATCATCAAG GGCGGTTCACCATCTCCGGGACACGCCAAGAACCACTGTACCTGCAGATGTCTCCCTGAA GTCCGAGACACCGCCATGTACTACTGACCGGGCTTCCCTCTGTGAGACACGGGCGCATGG ATTACTGGGCGCTGGCACCTCTGTGACCGTGTCTCTGGCGAGGGGAGTGGAGGCGGAGGA AGTGGAGGGGGGATCCGACATCCAGATGACCCAGTCCCCAAGTTATGTCCACCTCCGTGGG CGACAGAGTGTCCGTGACCTGCAAGGCTCCAGAACAGTGGACACCAACGTGGCTGGTATCAGC AGAAGCCCGCCAGTCCCTAAGGCCCTGATCTACTCCGCTCTCTACCGGTACTCTGACGTGCCT GACCGGTTACCGGCTCCGAGTCCGGCACCGACTTACCTTACCTTCCAAACGTGCAGTCTGA GGACCTGGCGGAGTACTTCTGCCAGCAGTACGACTCTACCTTACACCTTCGGCGGAGGAGCA AGCTGGAATCAAGTCCGGAGGTGGTGGATCCGAGGTGCAGTGGTCTGAGGAGGAGTGTG

401.	PSMA-4 L	artificial	aa	GTGCAGCCTGGAGGTCATTGAAACTCTCATGTGAGCCCTTGATTCACTTCAATAAGTACGC CATGAACCTGGTCCGCCAGGCTCCAGGAAGGTTTGAATGGTTGCTCGCATAGAAGTAAAT ATAATAATTATGCAACATATATATGCCGATTCAAGTGAAGACAGGTTACCATCTCCAGAGATGAT TCAAAAAACACTGCCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTACTACTG TGTGAGACATGGGAACCTTCGGTAATAGCTACATATCTTACCTGGCTTACTGGGGCCAGGCACTC TGGTACCGTCTCCTCAGGTGGTGGTGTCTGGCGGGCGGCTCCGGTGGTGGTGGTGGTGGTGG ACTGTTGTGACTCAGGAACCTTCACTACCGTATCACTGGTGAACAGTCACTCACTACTGGTGG CTCCTCGACTGGGCTGTACATCTGGCAACTACCAAACTGGTCCAAACAAACAGTCAAGG CACCCGTGGTCTAATAGTGGGACTAGTTCCTCGCCCCGGTACTCCTGCCAGATTCTCAGGC TCCCTGCTTGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGGATGAGGAGAAATA TTACTGTGTTCTATGGTACAGCAACCGTGGTGTTCGGTGGAGGAACCAAACTGACTGCTCTA DIELTQSPSLPVLGDQASISCRSSQSLVHSGNTYLHWFLQKPGQSPKLLIYTVSNRFSGVDP RFGSGSGTDFTLKISRVEAEDLGVYFCSQSTHVPFTFGGKLEIK
402.	PSMA-4 L	artificial	nt	GACATCGAGCTGACCCAGTCCCGCTGCTCCCTGCTGTGATCCTGGCGACCCAGGCTCCATCTC CTGCCGTCTCCAGTCCCTGGTGCATCAACGGCAATACTACCTGCACTGGTTCTGTCAGA AGCTTGGCCAGTCCCTAAGCTGCTGATCTACACCGTGTCCAAACGGTTCTCCGGGTGCTGAC AGGTTCTCTGGCTCCGGCTCCGGCACCGACTTCACTTGAAGATCTCCCGGTGGAGCCGAAGA TCTGGCGGTGACTTTTGTCTCCAGTCCACCCACGTCGCTACCTTCGGCGGAGGACCAAGCTGG AAATCAAG
403.	PSMA-4 LCDR1	artificial	aa	RSSQSLVHSGNTYLH
404.	PSMA-4 LCDR2	artificial	aa	TVSNRFS
405.	PSMA-4 LCDR3	artificial	aa	SQSTHVP
406.	PSMA-4 H	artificial	aa	QVQLQQSGAELVEPGASVKLSCKASGYFTFTYFDINWLRQRPEQGLEWIGGISPGDGNINYNENFK GKATLTIDKSSTTAYIQLSRLTSEDSAVYFCARDGNFPYAMDWSGQGTSTVSS
407.	PSMA-4 H	artificial	nt	CAGGTGAGCTGCAGCAGTCTGGCGCCGAACTGGTGGAGCCTGGCGCTCCGTGAAGCTGCTCTG CAAGGCTCCGGCTACACTTCACTACTCGACATCAACTGGCTGGCGCAGAGGCCCTGACGAGG GCCTGGAATGGATCGCGGCGCATCTCCCTGGGACGGCAACCACTACACAGAGACTTCAAG GGCAAGGCCACCTGACCATCGACAAGTCTCCACACCGCTACATCCAGCTGTCCCGGTGAC CTCTGAGGACTCCGCCGTGACTTCTGGCGCAGGACGGCAACTTCCCTTACTACGCCATGGACT CTGGGCGCAGGCGACCTCCGTGACCGTGTCTAGT
408.	PSMA-4 HCDR1	artificial	aa	YFDIN
409.	PSMA-4 HCDR2	artificial	aa	GLSPGDGNINYNENFKG
410.	PSMA-4 HCDR3	artificial	aa	DGNFPYAMD
411.	PSMA-4 HL	artificial	aa	QVQLQQSGAELVEPGASVKLSCKASGYFTFTYFDINWLRQRPEQGLEWIGGISPGDGNINYNENFK GKATLTIDKSSTTAYIQLSRLTSEDSAVYFCARDGNFPYAMDWSGQGTSTVSSGGGGGGGGS GGGSDIELTQSPSLPVLGDQASISCRSSQSLVHSGNTYLHWFLQKPGQSPKLLIYTVSNRF

412.	PSMA-4 HL	artificial	nt	<p>SGVDFRFGSGSGTDFTLKI SRVEAEDLVFCQSQSTHVPTFGGKLEIK</p> <p>CAGGTGCAGCTGCAGCAGTCTGGCGCGAACTGGTGGAGCCTCGCTCCGTGAAGCTCTCTG CAAGGCCTCCGGCTACACCTTACCTACTCGACATCAACTGGCTGGCGAGAGCCCTGAGCAGG GCCTGGAATGGATCGGCGCATCTCCCTGGCGACGGCAACCACTACAACGAGAACTTCAAG GGCAAGCCACCTGACCATCGACAAGTCTCCACACCGCTACATCCAGCTGTCCCGCTGAC CTCTGAGGACTCCGCCGTGACTTCTGGCGAGGACGGCAACTTCCCTTACTACGCATGGACT CTTGGGCCAGGCACCTCCGTGACCGTGTCTAGTGGCGGAGGATCTGGCGGAGGGGATCT GGGGCGGAGGAAGCAGCATCGAGCTGACCCAGTCCCCCTGTCCCTGTGATCTCTGGCGA CCAGGCCTCATCTCCTGCCGTCTCCAGTCCCTAAGCTGTGATCTACACCGTGTCCAACCGGTT ACTGGTTCTGCAGAAGCCTGGCCAGTCCCTAAGCTGTGATCTACACCGTGTCCAACCGGTT TCCGGCTGCTGACAGGTTCTCTGGCTCCGGCTCCGACCGACTTCAACCTGAAGATCTCCCG GGTGAGGCCGAAGATCTGGCGGTGACTTCTGCTCCAGTCCACCCAGTGCCTACCTTCGGCG GAGGACCAAGCTGGAATCAAG</p>
413.	PSMA-4HL x I2C HL	artificial	aa	<p>QVQLQSGAELVEPGASVKLSCKASGYTFYFDINWLQRPEQGLEWIGGISPGDGNINYNENFK GKATLTIDKSTTAYIQLSRLTSEDSAVYFCARDGNFPYYAMDSWGQTSVTVSSGGSGSGGGS GGGSDIELTQSPILPVIILGDAQSISCRSSQSLVHSNGNTYLHWFLQKPGQSPKLLIYTVSNRF SGVDFRFGSGSGTDFTLKI SRVEAEDLVFCQSQSTHVPTFGGKLEIKSGGGGSEVQLVESG GGLVQPGGSLKLSAASGFTFNKYAMNWRQAPKGLSEWVARIRSKYNNYATYYADSVKDRFTIS RDSKNTAYLQMNLLKTEDTAVYYCVRHGNEFNSYISYWAYWGQTLTVTVSSGGSGSGGSGGG GSQTVVTEPSLTVSPGGTVTLTCCSSTGAVTSGNYPNWWQKPKQAPRGLIGGTFKFLAPGTPAR FSGLLGGKAALTLSGVQPEDEAEYYCVLWSNRWVFGGKLTIVL</p>
414.	PSMA-4HL x I2C HL	artificial	nt	<p>CAGGTGCAGCTGCAGCAGTCTGGCGCGAACTGGTGGAGCCTGGCGCCTCCGTGAAGCTCTCTG CAAGGCCTCCGGCTACACCTTACCTACTCGACATCAACTGGCTGGCGAGAGCCCTGAGCAGG GCCTGGAATGGATCGGCGCATCTCCCTGGCGACGGCAACCACTACAACGAGAACTTCAAG GGCAAGCCACCTGACCATCGACAAGTCTCCACACCGCTACATCCAGCTGTCCCGCTGAC CTCTGAGGACTCCGCCGTGACTTCTGGCGAGGACGGCAACTTCCCTTACTACGCATGGACT CTTGGGCCAGGCACCTCCGTGACCGTGTCTAGTGGCGGAGGATCTGGCGGAGGGGATCT GGGGCGGAGGAAGCAGCATCGAGCTGACCCAGTCCCCCTGTCCCTGTGATCTCTGGCGA CCAGGCCTCATCTCCTGCCGTCTCCAGTCCCTGAGTGTGATCTACACCGTGTCCAACCGGTT ACTGGTTCTGCAGAAGCCTGGCCAGTCCCTAAGCTGTGATCTACACCGTGTCCAACCGGTT TCCGGCTGCTGACAGGTTCTCTGGCTCCGGCTCCGACCGACTTCAACCTGAAGATCTCCCG GGTGAGGCCGAAGATCTGGCGGTGACTTCTGCTCCAGTCCACCCAGTGCCTACCTTCGGCG GAGGACCAAGCTGGAATCAAGTCCGAGGAGTGGTGGATCCGAGTGCAGTGGTCGAGTCTGGA GGAGATTGGTGCAGCCTGGAGGTCATTGAACTCTCATGTGAGCCCTCTGGATTACCTTCAA TAAGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGGTTTGGATGGTGTCTCGCATAA GAAGTAAATATAATAATTATGCAACATATTATGCCGATTTCAGTGAAAGACAGGTTTCAACCTCC AGAGATGATTCAAAAAACACTGCCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGT</p>

				GTACTACTGTGTGAGACATGGGAACCTCGGTAAATAGTACATATCTACTGGGCTTACTGGGOC AAGGACTCTGGTCAACCGTCTCCTCAGGTGGTGGTGTCTGGCGGGGGCTCCGGTGGTGGT GGTCTCAGACTGTTGTGACTCAGGAACCTTCACTACCGTATCACCTGGTGAACAGTCAACT CACTTGTGGTCTCTCGACTGGGCTGTACATCTGCACTACCAAACTCCAACTCCCTCCAGA CAGTCAGGCACCCCGTGGTCTAATAGGTGGGTAAGTCTCTGCCCCCGGTACTCTCCCTGGA TTCTCAGGCTCCCTGCTTGGAGGCAAGGTGCGCTACCGCTCTCAGGGTACAGCCAGAGATGA GGCAGAAATATTACTGTGTTCTATGGTACAGCAACCGTGGGTGTTCTGGTGGAGAACCAAACTGA CTGTCTCTA
415.	PSMA-6 L	artificial	aa	DIKMTQSPSSMYASLGERVTITCKASQDIYSYLIIWFQKPKSPKTLIYRANRLVDGVPSRFSGS GSGQDYSLTIISSLEYEDMGIYYCLQYDEFATFGSGTKLEMK
416.	PSMA-6 L	artificial	nt	GACATCAAGATGACCCAGTCCCCCTCTCCATGTACGCTCCCTGGCGGAGAGATGACCATCAC CTGCAAGGCTCCAGGACATCTACTCTACTGATCTGGTCCAGCAGAACCTGGCAAGTCCC CTAAGACCTGATCTACCGGGCCACAGACTGGTGACGGCTGCTTCCAGGTTCTCCGGCTCC GGCTCTGGCCAGGACTACTCCCTGACCATCTCTCTCCCTGGAATACGAGGACATGGGATCTACTA CTGCTGCAGTACGACGAGTTCGCCACCTTCGGCTCCGGCACCAAGCTGGAATGAAG
417.	PSMA-6 L CDR1	artificial	aa	KASQDIYSYLI
418.	PSMA-6 L CDR2	artificial	aa	RANRLVD
419.	PSMA-6 L CDR3	artificial	aa	LQYDEFAT
420.	PSMA-6 H	artificial	aa	DVHLQESGPGLVKPSQSLSTCTVTGYSITSDYANNWIRQFPGNKLEWMGYISFSGSTSYNPSLK SRI SVTRDTSKNQFFLQNLNVTTEDTATYICARWNYGSSHVWFAYWGQGLIVTSS
421.	PSMA-6 H	artificial	nt	GACGTGCACCTGCAGGAATCTGGCCCTGGCTGGTGAAGCTTCCCAGTCCCTGTCCCTGACCTG CACCGTGACCGGCTACTCCATCACCTCCGACTACGCTGGAACCTGGATCCGGCAGTCCCTGGCA ATAAGCTGGAATGGATGGCTACATCTCTCTCCGGCAGCACCTCCTACACCCCTCCCTGAAG TCCCGGATCTCCGTGACCCGGGACACCTCCAAGAACCAAGTCTTCTCTGAGCTGAACCTCGTGAC CACCGAGGACACCGCCACCTACTACTGCGCCGGTGGAACTACTACGGCTCCTCCCACTGTGGT TCGCTTACTGGGGCCAGGCAACCTGGTGACCGTGCTCTCTCC
422.	PSMA-6 H CDR1	artificial	aa	SDYAWN
423.	PSMA-6 H CDR2	artificial	aa	YISFSGSTSYNPSLKS
424.	PSMA-6 H CDR3	artificial	aa	WNYGSSHVWFAY
425.	PSMA-6 LH	artificial	aa	DIKMTQSPSSMYASLGERVTITCKASQDIYSYLIIWFQKPKSPKTLIYRANRLVDGVPSRFSGS GSGQDYSLTIISSLEYEDMGIYYCLQYDEFATFGSGTKLEMKGGGGGGGGSDVHLQESGP GLVKPSQSLSTCTVTGYSITSDYANNWIRQFPGNKLEWMGYISFSGSTSYNPSLKSRI SVTRDT SKNQFFLQNLNVTTEDTATYICARWNYGSSHVWFAYWGQGLIVTSS
426.	PSMA-6 LH	artificial	nt	GACATCAAGATGACCCAGTCCCCCTCTCCATGTACGCTCCCTGGCGGAGAGATGACCATCAC CTGCAAGGCTCCAGGACATCTACTCTACTGATCTGGTTCAGCAGAACCTGGCAAGTCCC CTAAGACCTGATCTACCGGGCCACAGACTGGTGGACGGCTGCTTCCAGGTTCTCCGGCTCC

<p>GGCTCTGGCCAGGACTACTCCCTGACCAICTCTCCCTGGAATACGAGACATGGGCATCTACTA CTGCTGCAGTACGACGAGTTCGCCACCTTCGGCTCCGGCACCAGCTGAAATGAAGGGGGAG GGGATCTGGCGGGAGGAAGTGGGGGGAGGATCCGACGTGCACCTGCAGGAATCTGGCCT GGCTGGTGAAGCCTTCCCAGTCCCTGTCCTGACCTGCACCGTACCGGCTACTCCATCACCTC CGACTACGCCTGGAACCTGGATCCGGCAGTTCCTTGGCAATAAGCTGGAATGGATGGGCTACATCT CCTTCTCCGGCAGACCTCTCTACAACCTTCCCTGAACTCCCGATCTCCGTGACCCCGGACACC TCCAAGAACCACTTCTCTGACGTGAACCTCCGTGACCAACCGAGGACACCGCCACCTACTACTG CGCCGGTGGAACTACTACGGCTCTCCCACTGCTGGTTCGCTTACTGGGGCCAGGGCACCCCTGG TGACCGTGTCTCTCC</p>				<p>DIKMTQSPSSMYASLGERVTITCKASQDIYSLIWFQKPKSPKTLIYRANRLVDVPSRFSGS GSGQDYSLTISSLEYEDMGIYYCIQYDEFATFGSGTKLEMKGGSGGGSDVHLQESGP GLVKPSQSLTCTVTGYSITSDYANNWIRQPPGNKLEWMGYISFSGSTSYNPSLKSRIISVTRDT SKNQFELQLNSVTEDTATYYCARWNYGSSHVWFAYWQGLTVTVSSGGGSEVQLVESGGGLV QPGSLKLSCAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYYADSVKDRFTISRDDS KNTAYLQMNLLKTEDTAVYYCVRHGFNSYISYWAYWQGLTVTVSSGGSGGGSGGGSGQT VVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQKPKGQAPRGLIGTKFLAPGTPARFSGS LLGKAALTLSGVQPEDEAEYYCVLWYNRWVFGGTKLTVL</p>
<p>427. PSMA-6 LH x l2C HL</p>	<p>aa</p>	<p>artificial</p>		<p>nt</p>
<p>428. PSMA-6 LH x l2C HL</p>		<p>artificial</p>		<p>GACATCAAGATGACCCAGTCCCTCTCTCATGTACGCTCCCTGGCGGAGAGAGTACCATCAC CTGCAAGCCTCCCAGGACATCTACTCTCTACTGATCTGGTTCAGCAGAAAGCCTGGCAAGTCCC CTAAGACCCCTGATCTACCGGGCCAAACAGACTGGTGGACGGCTCCCTCCAGTCTCCGGCTCC GGCTTGGCCAGGACTACTCCCTGACCATCTCTCCCTGGAATACGAGGACATGGGCATCTACTA CTGCCTGCAGTACGACGAGTTCGCCACCTTCGGCTCCGGCACCAGCTGGAATGAAGGGCGGAG GGGATCTGGCGGGGAGGAAGTGGGGGGGAGGATCCGACGTGCACCTGCAGGAATCTGGCCT GGCCTGGTGAAGCCTTCCCAGTCCCTGTCCCTGACCTGCACCTGACCGGCTACTCCATCACCTC CGACTACGCTGGAACCTGGATCCGGCAGTTCCTTGGCAATAAGCTGGAATGGATGGGCTACATCT CCTTCTCCGGCAGCACCTCTACACCTTCCCTGAACTCCCGGATCTCCGTGACCCGGGACACC TCCAAGAACCACTTCTCTGACGTGAACCTCCGTGACCAACCGAGGACACCGCCACCTACTACTG CGCCGGTGAACCTACTACGGCTCTCCCACTGCTGGTTCGCTTACTGGGGCCAGGGCACCCCTGG TGACCGTCTCTCCGAGGTGGTGGATCCGAGGTGAGTGGTTCGCTTACTGGGGCCAGGGCACCCCTGG CAGCCTGGAGGGTCATTGAACTCTCATGTGAGCTCTGGATTCACCTTCAATAAGTACGCCAT GAACTGGGTCCGCCAGGCTCCAGGAAAGGGTTTGAATGGGTTCGTCGATAAGAAGTAATATA ATAATTATGCAACATATTATGCCGATTTCAGTGAAGACAGAGTTTACCATTCCAGAGATGATTCA AAAACACTGCCTATCTACAAATGAACAACCTGAAAACCTGAGGACACTGCCGTGTACTACTGTGT GAGACATGGGAACCTTCGGTAATAGCTACATATCTACTGGGCTTACTGGGGCCAAAGGACTGTGG TCACCGTCTCTCAGGTGGTGGTTCCTGGCGGGCGGGCTCCGGTGGTGGTTCCTCAGACT GTTGTGACTCAGGAACCTTCACTACCGGTATCACCTGGTGGAAACAGTCACTCACTTGTGGCTC CTCGACTGGGCTGTACATCTGGCAACTACCCAAAGTGGTCCAAACAAACAGGTGACGGCAC</p>

					CCCGTGGTCTAATAGGTGGGACTAAGTTCCTGCCCCCGGTACTCTGCCAGATTCTCAGGCTCC CTGCTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCAGGATCAGGCAAGATATTA CTGTGTTCTATGGTACAGCAACCGCTGGGTGTTGGTGGAGAACCAAACTGACTGTCTTA
429.	PSMA-7 L	artificial	aa		DIVMTQSHKFMSTSVGDRVSIICKASQDVGTAVDWYQQKPGQSPKLLIYWASTRHTGVPDRFTGS GSGTDFTLITINQSEDLADYFCQQYNSYPLTFGAGTMDLK
430.	PSMA-7 L	artificial	nt		GACATCGTGATGACCCAGTCCCAAGTTTCATGTCACCTCCGTGGGCGACCGGGTGTCCATCAT CTGCAAGGCCCTCCAGGATGTGGCAACCGCTGGACTGGTATCAGCAGAACCTGGCCAGTCCC CTAAGCTGCTGATCTACTGGGCTCCACAGACACCGGCTGCTGACAGATTCAACGGCTCC GGCTCTGGCACCGACTTCAACCTGACCATCAACACGTGACGTCGAGGACCTGGCCGACTACTT CTGCCAGCAGTACAACCTCCTACCTCTGACCTTCGGGCTGGACCATGCTGGACCTGAAG
431.	PSMA-7 LCDR1	artificial	aa		KASQDVGTAVD
432.	PSMA-7 LCDR2	artificial	aa		WASTRHT
433.	PSMA-7 LCDR3	artificial	aa		QQYNSYPLT
434.	PSMA-7 H	artificial	aa		EVQLQQSGPELVKPGTSVIRISCKTSGYTFTEYTIHWVKQSHGKSLEWIGNINPNNGGTTYNQKFE DKATLTVDKSSSTAYMELRSLTSEDSAVYYCAAGWNFDYWGQGITLVSS
435.	PSMA-7 H	artificial	nt		GAAAGTGCAGCTGCAGCAGTCCGGCCCTGAGCTGGTGAAGCCTGGCACCTCCGTGCGGATCTCTTG CAAGACCTCCGGCTACACCTTCACCGAGTACACATCCACTGGGTGAACAGTCCACAGCAAGT CCCTGGAATGGATCGGCAACATCAACCTTAACAGCGGCGCACCACTACAACAGAACTCGAG GACAAGGCCACCTTGACCGTGGCAAGTCTCTCCACCGCTACATGGAACTCGGGTCCCTGAC CTCCGAGGACTCCGCCGTGACTACTGCGCGCTGGCTGGAACCTCGACTACTGGGGGCCAGGCA CCACACTGACCGTGTCTCTCC
436.	PSMA-7 HCDR1	artificial	aa		EYTIH
437.	PSMA-7 HCDR2	artificial	aa		NTNPNGGTTYNQKFED
438.	PSMA-7 HCDR3	artificial	aa		GWNFYD
439.	PSMA-7 LH	artificial	aa		DIVMTQSHKFMSTSVGDRVSIICKASQDVGTAVDWYQQKPGQSPKLLIYWASTRHTGVPDRFTGS GSGTDFTLITINQSEDLADYFCQQYNSYPLTFGAGTMDLKGGGSGGGGSEVQLQQSG PELVKPGTSVIRISCKTSGYTFTEYTIHWVKQSHGKSLEWIGNINPNNGGTTYNQKFEDKATLTVD KSSSTAYMELRSLTSEDSAVYYCAAGWNFDYWGQGITLVSS
440.	PSMA-7 LH	artificial	nt		GACATCGTGATGACCCAGTCCCAAGTTTCATGTCACCTCCGTGGGCGACCGGGTGTCCATCAT CTGCAAGGCCCTCCAGGATGTGGGCAACCGCTGGACTGGTATCAGCAGAACCTGGCCAGTCCC CTAAGCTGCTGATCTACTGGGCTCCACAGACACACCGGCTGCTGACAGATTCAACGGCTCC GGCTCTGGCACCGACTTCAACCTGACCATCAACAGTGCAGTCCGAGGACCTGGCCGACTACTT CTGCCAGCAGTACAACCTCCTACCTCTGACCTTCGGGCTGGACCATGCTGGACCTGAAGGCGG GAGGGGGCTCTGGCGGCGGAGGAGTGGAGGGGGGATCCGAAGTGCAGCTGCAGCAGTCCGGC CCTGAGCTGGTGAAGCCTGGCACTCCGTGGGATCTCTTGAAGACCTCCGGCTACACTTCAC CGAGTACACCATCCACTGGGTGAACAGTCCACGGCAAGTCCCTGGATGGATCGGCAACATCA

				441.
PSMA-7 LH x l2C HL	artificial	aa		
PSMA-7 LH x l2C HL	artificial	nt		442.
PSMA-8 L	artificial	aa		443.
PSMA-8 L	artificial	nt		444.

ACCCTAACAAACGGCGGCACACCTACAAACAGAAAGTTCGAGGACAAGGCCACCCCTGACCGTGGAC
 AAGTCTCTCCACCGCTACATGGAACCTGGGTCCCTGACCTCCGAGGACTCCGCCGTACTA
 CTGCGCGCTGGCTGGAACCTCGACTACTGGGCCAGGCACACACTGACCGTGTCTCC
 DIVMTQSHKFMSTSVGDRVSIICKASQDVGTAVDWYQQKPGQSPKLLIYWASTRHTGVDFRTGS
 GSGTDFTLTIITNVQSEDLADYFCQQYNSPLTEGAGTMLDLKGGSGGGGGSEVQLQQSG
 PELVKPGTSVRISCKTSGYTFEYTIHWVKQSHKSLKSLWIGININPNNGGTTYNQKFEKATLITVD
 KSSSTAYMEILRLTSEDSAVYYCAAGWNEDYWGQGTTLTVSSGGGSEVQLVESGGGLVQPQGS
 KLSCAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYADSVKDRFTISRDDSKNTAYL
 QMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQTLTVSSGGGSGGGGGSTVVTQEP
 SLTVSPGGTTLTTCGSSTGAVTSGNYPNWPVQKPGQAPRGLIGTKFLAPGTPARTSGSLGGKA
 ALTLGVQPEDEAEIYCVLWYSNRWVFGGTKLTVL
 GACATCGTGATGACCCAGTCCCAAGTTTCATGTCCACCTCCGTGGCGACCGGGTGTCCATCAT
 CTGCAAGGCCTCCCAGGATGTGGGCACCGCGTGGACTGGTATCAGCAGAAAGCTGGCCAGTCCC
 CTAAGCTGTGATCTACTGGCCCTCCACGACACACCGCGTGCCTGACAGATTACCGGCTCC
 GGCTCTGGCACCGACTTCACCTGACCATCACCACGTCAGTCCGAGGACCTGGCCGACTACTT
 CTGCCAGCAGTACAACTCCTACCTCTGACCTCGGCGCTGGCACCATGCTGGACCTGAAGGCG
 GAGGGGCTCTGGCGGCGAGGAGTGGGGGCGGATCCGAAGTGCAGCTGCAGGAGTCCGGC
 CCTGAGCTGGTGAAGCCTGGCACCTCCGTGGGATCTTTCAAGACCTCCGGTACACCTTCAC
 CGAGTACACCATCCACTGGGTGAACAGTCCACGCAAGTCCCTGGAATGGATGGCAACATCA
 ACCCTAACACGGCGGCACCATACACACAGAAATTCGAGGACAAGGCCACCTGACCGTGGAC
 AAGTCTCTCCACCGCTACATGGAACCTGGTCCCTGACCTCCGAGGACTCCGCCGTGTACTA
 CTGCGCGCTGGCTGGAACCTCGACTACTGGGCGCAGGCACACACTGACCGTGTCTCCGAG
 GTGGTGGATCCGAGGTGCAGCTGGTGCAGTCTGAGTCTGAGGAGGATTGGTGCAGCCTGGAGGCTATTG
 AAACTCTCATGTGCAGCCTCTGGATTCACTTCAATTAAGTACGCCATGAACCTGGTCCGCGAGGC
 TCCAGGAAAGGGTTTGAATGGGTGCTCGCATGAAGTAAATATAATAATATGCAACATATT
 ATGCCGATTCACTGAAAGACAGGTTCACTTCCAGAGATGATTCAAAAACACTGCCATCTA
 CAAATGAACAACTTGAAACTGAGGACACTGCGGTGACTACTGTGTGAGACATGGGAACTTCGG
 TAAATAGCTACATATCCTACTGGCTTACTGGGCGCAAGGACTCTGGTACCGTCTCTCAGGTG
 GTGGTGGTTCTGGCGCGCGCTCCGGTGGTGGTGTCTCAGACTGTGTGACTCAGGAACCT
 TCACTACCGTATCACTGGTGAACAGTCACTCACTTGTGGTCTCTGACTGGGCTGTAC
 ATCTGGCAACTACCCAACTGGGTCCAAACAAAACAGGTCAGGCACCCCGTGGTCTAATAGGTG
 GGAATAAGTTCCTGCGCCCGGTACTCCTGCCAGATCTCAGGCTCCCTGCTTGGAGGCAAGGCT
 GCCCTACCCCTCAGGGGTACAGCCAGAGGATGAGCAGAAATATTACTGTCTTATGTGTACAG
 CAACCGCTGGGTGTTCCGTGGAGAACCAACTGACTGTCTTA

DIVLTQSPASLAVSLGQRATISCRASESIDSYNTFMHWYQKPGQPPNLLIFRASIILESGIPAR
 FSGSGSGTDFTLTITIPVEADDAVYYCHQSIEDPYTFGGGTKLEIK
 GACATCGTGTGACCCAGTCTCCAGCCTCCCTGGCTGTGTCTCTGGGCCAGCGGGCCACCATCTC

				TTGCCGGGCTCCGAGTCCATCGACTCCTACGACAACACCTTCATGCACTGGTATCAGCAGAAGC CTGGCAGCCTCCTAACCTGCTGATCTTCGGGCTCTATCGGAATCCGGCATCCCTGCCGG TTCTCCGGCTCTGGCTCCGGCACCAGCTTACCTTGACCTGACCACTACCTTGTGGAGGCCAGACGT GGCCACCTACTACTGCCACCACTCCATCGAGGACCTTACACCTTCGGCGGAGGGACCAAGCTGG AAATCAAG
445.	PSMA-8 LCDR1	artificial	aa	RASEIDSNDTFMH
446.	PSMA-8 LCDR2	artificial	aa	RASILES
447.	PSMA-8 LCDR3	artificial	aa	HQSIEDPYT
448.	PSMA-8 H	artificial	aa	EVQLQSGPELVKPGASVKMSCKASGYFTGYVMHWVKQPGQVLEWIGYINPYNDVTRYNGKFK GKATLTSVKYSSTAYMELSLTSEDSAVYVCARGENWYFDSWGRGATLVSS
449.	PSMA-8 H	artificial	nt	GAAGTCAGCTGCAGCAGTCCGGCCCTGAGCTGGTGAAGCCTGGCCCTCCGTGAAGATGTCCTG CAAGCCTCCGGCTACACCTTACCGGTACGTGATGCACTGGTGAACAGAAACCGGCCAGG TGCTGGAATGGATCGGCTACATCAACCTTACACGACGTGACCCGTACAACGGCAAGTTCAAG GGCAAGGCCACCTGACCTCCGACAAGTACTCTCCACCGCTACATGGAAGTGTCCGGCTGAC CTCTGAGGACTCCGCCGTGTACTACTGCGCAGGGCGGAGAACTGGTACTACTTCGACTCCTGGG GCAGAGCGCTACCTGACCGTGTCTTCC
450.	PSMA-8 HCDR1	artificial	aa	GYVMH
451.	PSMA-8 HCDR2	artificial	aa	YINPYNDVTRYNGKFKG
452.	PSMA-8 HCDR3	artificial	aa	GENWYFDS
453.	PSMA-8 LH	artificial	aa	DIVLTQSPASLAVSLGQRATISCRASEIDSNDTFMHWYQKPGQPNLLIFRASILESGIPAR FSGSGSTDFLTIIYPVEADVATYYCHQSIEDPYTFGGGKLEIKGGSGGGGGGGSEVQL QQSGPELVKPGASVKMSCKASGYFTGYVMHWVKQPGQVLEWIGYINPYNDVTRYNGKFKGKAT LTSDKYSSTAYMELSLTSEDSAVYVCARGENWYFDSWGRGATLVSS
454.	PSMA-8 LH	artificial	nt	GACATCGTGTGACCCAGTCTCCAGCTCCCTGGCTGTGTCTCTGGCCAGCGGGCCACCATCTC TTGCCGGGCTCCGAGTCCATCGACTCCTACGACACACCTTCATGCACTGGTATCAGCAGAAGC CTGGCAGCCTCCTAACCTGCTGATCTCCGGCTCTATCTGGAATCCGGCATCCCTGCCCGG TTCTCCGGCTCTGGCTCCGGCACCGACTTACCTGACCATCTACCTGTGGAGGCGACGACGT GGCCACCTACTACTGCCACCACTCCATCGAGCACCTTACACCTTCGGCGGAGGACCAAGCTGG AAATCAAGGGCGGAGGGGATCTGGCGGCGGAGGAAGTGGAGGGGGGATCCGAAGTGCAGCTG CAGCAGTCCGGCCCTGAGCTGGTGAAGCTCCGCTCCGTGAGATGTCTCGCAGGCTCCGG CTACACCTTCAACGGCTACGTGATGCACTGGTGAACAGAAACCCGGCCAGGTGTGGAATGGA TOGGTACATCAACCTTACAACGACGTGACCCGTTACACGGCAAGTTCAAGGGCAAGGCCACC CTGACCTCCGACAAGTACTCTCCACCGCTACATGGAAGTGTCCGGCTGACCTGAGGACTC CGCGGTGTAATACTGCGCCAGGGCGGAGAACTGGTACTACTTCGACTCTCTGGGCGAGAGCGGCTA CCCTGACCGTGTCTTCC
455.	PSMA-8 LH x I2C	artificial	aa	DIVLTQSPASLAVSLGQRATISCRASEIDSNDTFMHWYQKPGQPNLLIFRASILESGIPAR

	HL			<p>FSGSGGTDFTLTITYPEADDAVATYYCHQSIEDPYTFGGGKTLEIKGGGGGGGGGGSEVQL QSGPELVKPGASVKMSCKASGYFTGYVMHWKQKPGQVLEWIGYINPYNDVTRYNGKFKKAT LTSKYSSTAYMELSLTSEDNAVYICARGENWYFYFDSWGRGATLTVSSGGGGSEVQLVSGGGL VQPGSLKLSAASGFTFNKYAMNWVRQAPGRGLEWVARIRSKYNNYATYYADSVKDRFTISRDD SKNTAYLQMNLIKTEDAVYYCVRHGNFNSYISYWAYWQGTILVTVSSGGGGGGGGGGSSQ TVVTEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWQKPGQAPRGLIGGTKFLAPGTPARFSG SLLGKKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGTKLTVL</p>
456.	PSMA-8 LH x I2C HL	artificial	nt	<p>GACATCGTGTGACCCAGTCTCCAGCTCCCTGGCTGTGTCTCTGGGCCAGGGGCCACCATCTC TTGCCGGGCTCCGAGTCCATCGACTCCTACGACACACACCTTCATGCATGGTATCAGCAGAAGC CTGGCCAGCTCCTAACCTGTGATCTCCGGGCTCTATCCTGGAATCCGGCATCCTCCTCCCGG TTCTCCGGCTTGCTCCGGCACCGACTTCACCTGACCATCTACCTGTGGAGGCCGACACGCT GGCCACTACTACTGCTCCAGTCCATCGAGACCTTACACCTTCGGCGGAGGACCAAGCTGG AAATCAAGGGCGAGGGGATCTGGGGGGAGGAAGTGGAGGGGGGATCCGAAGTCCAGCTG CAGAGTCCGGCCCTGAGTGGTGAAGCTGGCGCTCCGTGAAGTGTCTGCAAGGCTCCGG CTACACCTTCCCGGCTACGTGATGCTGCTGGTGAACAGAAACCCGGCCAGTCTTGAATGGA TCGGCTACATCAACCTTACAACGAGTGCCTGCTGTAACGGCAAGTTCAGGGCAAGGCCACC CTGACCTCCGACAGTACTCTCCACCGCTACATGTAAGTCTCCGGCTGACCTCTGAGGACTC CGCGTGTACTACTGCGCCAGGGCGAGAACTGGTACTACTTCGACTCTCGGGCAGAGGCGCTA CCCTGACCGTGTCTTCCGAGGTGGTGGATCCGAGGTGCAGTGGTGCAGTCTGGAGAGGATTG GTGACGCTGGAGGCTATTGAACCTCTCATGTGCAGCTCTGGATTCACTTCAATTAAGTACGC CATGAAGTGGTCCGGCCAGCTCCAGGAAGGGTTTGAATGGTGTCTCGCATAGAAGTAAAT ATAATAATTATGCAACATATATGCCGATTCAAGTGAAGACAGTTTCACTCTCCAGAGATGAT TCAAAAACACTGCCTATCTACAAATGAACAATTTGAAACTGAGGACACTGCCGTGTACTACTG TGTGAGACATGGGAATTCGGTAATAGCTACATATCTTACTGGCTTACTGGGGCCAGGGACTC TGCTACCGTCTCCTCAGGTGGTGGTGTCTGGCGGGCGGCTCCGGTGGTGGTGTCTCTCAG ACTGTTGTGACTCAGGAACCTTCACTACCGTATCACTGGTGGAAACAGTCACTACTGTGTGG CTCCTCGACTGGGCTGTACATCTGGCAACTACCCAAACTGGTCCAAACAAACAGGTCAGG CAGCCGTGGTCTAATAGTGGGACTAAGTCTCTCGCCCCGGTACTCCTCCAGATCTCTCAGGC TCCCTGCTTGGAGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGCAGAATA TTACTGTGTTCTATGTTACAGCAACCGCTGGTGTTCGGTGGAGGAACCAACTGACTGTCTTA NIVMTQSQKFMSTSPGDRVRVTCKASQNVSDVAVYQAKPGQSPRILISTSYRYSVGPDRFTAY GSGTDFTLTITNVQSEDLTEYFCQQYNLYPLTFAGTKLELK</p>
457.	PSMA-9 L	artificial	aa	
458.	PSMA-9 L	artificial	nt	<p>AACATCGTGATGACCCAGTCCAGAAATTCATGTCCACCTCTCCGGCGATAGAGTGCCTGAC CTGCAAGGCCTCCCAAGACGTGGCTCCGACGTGGCTGGTATCAGGCCAAGCCTGGCCAGTCCC CTCGGATCCTGTATCTACTCCACTCTACCGGTACTCCGGCTGCCTGACAGATTCACCCCTAC GGCTCCGGCACCGACTTCACTGACCATTAACAAACGTGCAGTCCGAGGACCTGACCCAGTACTT CTGCCAGCAGTACAACCTCCTACCTCTGACCTTCGGCGCTGGCAACCAAGCTGGAAGTGAAG</p>

459.	PSMA-9 LCDR1	artificial	aa	KASQNVGSDVA
460.	PSMA-9 LCDR2	artificial	aa	STSYRYS
461.	PSMA-9 LCDR3	artificial	aa	QQNSYPLT
462.	PSMA-9 H	artificial	aa	QVQLKESGPGLVASSQSLSITCTVSGFSLTAYGINWVRQPPGKGLEWLGVIWPDGNTDYNSTLKS RLNIFKDNQVFLKMSFQDDTARYFCARDSYGNFKRGWDFWQGTTLVSS
463.	PSMA-9 H	artificial	nt	CAGTGGAGCTGAAAGAGTCCGGCCCTGGCTGGTGGCTCTCCAGTCCCTGTCCATCACCTG CACCGTGTAGGCTTCTCCGTACCGCTTACGGCATCACTGGTGGCCAGCCTCCTGGCAAGG GCCTGGAATGGCTGGCGGTGATCTGGCTGACGGCAACACCGATACACAGCACCTTGAAGTCC CGGTGAACATCTTCAAGGACAACTCCAGAACACAGGTGTTCTTGAAGATGCTCTTCCAGAC CGACGACACCGCCCGGTACTTTTGGCCAGGACTCTACGGCAACTTCAAGCGGGCTGGTTCG ATTTTGGGGCCAGGGCACCACTGACCGTGTCTCC
464.	PSMA-9 HCDR1	artificial	aa	AYGIN
465.	PSMA-9 HCDR2	artificial	aa	VIWPDGNTDYNSTLKS
466.	PSMA-9 HCDR3	artificial	aa	DSYGNFKRGWDF
467.	PSMA-9 LH	artificial	aa	NIVMTQSQKFMSTSPGDRVRVTKASQNVGSDVAVYQAKPGQSPRILYSTSYRYSVGPDRFTAY GSGTDFTLTIINVQSEDLTEYFCQQYNSYPLTFGAGTKLELKGSGGGGGGGVQLKESG PGLVASSQSLSITCTVSGFSLTAYGINWVRQPPGKGLEWLGVIWPDGNTDYNSTLKSRLNIFKDN SKNQVFLKMSFQDDTARYFCARDSYGNFKRGWDFWQGTTLVSS
468.	PSMA-9 LH	artificial	nt	AACATCGTGATGACCCAGTCCCAGAAATTCATGTCCACCTCTCCGGCGATAGTGGCGGTGAC CTGCAAGGCGCTCCAGAACGTGGCTCCGACGTGGCTGGTATCAGGCCAAGCCTGGCCAGTCCC CTCGGATCCTGTGATCTACTCCACCTCCTACCGTACTCCGGCTGCTGACAGATTACCGCTAC GGTCCGGCACCGACTTCACTCCGTGACATTACAACTGCGAGTCCGAGGACCTGACCGAGTACTT CTGCCAGCAGTACAACTCTACCTCTGACCTTCGGCGCTGGCACCAGCTGGAATGAAAGGCGG GAGGGGCTCTGGCGGGAGGAAGTGGAGGGGGGGGATCTCAGGTGCAGCTGAAAGAGTCCGGC CCTGGCTGTGGCTCTCTCCAGTCCCTGTCTCATCACCTGCACTGCTCAGCTTCTCCCTGAC CGCTTACGGCATCACTGGTGGCCAGCCTCTGGCAAGGCGCTGGAATGGTGGCGGTGATCT GGCTGACGGCAACACCGACTACACAGCACCTGAACTCCCGCTGAACATCTTCAAGGACAAAC TCCAAGAACACAGGTGTTCTGAAGATGCTCTCTCCAGACCGACACCGCCGCTACTTTG CGCCAGGACTCTACGGCAACTTCAAGCGGGGCTGTTGCTGATTTTGGGGCCAGGGCACACAC TGACCGTGTCTCTCC
469.	PSMA-9 LH x 12C HL	artificial	aa	NIVMTQSQKFMSTSPGDRVRVTKASQNVGSDVAVYQAKPGQSPRILYSTSYRYSVGPDRFTAY GSGTDFTLTIINVQSEDLTEYFCQQYNSYPLTFGAGTKLELKGSGGGGGGGVQLKESG PGLVASSQSLSITCTVSGFSLTAYGINWVRQPPGKGLEWLGVIWPDGNTDYNSTLKSRLNIFKDN SKNQVFLKMSFQDDTARYFCARDSYGNFKRGWDFWQGTTLVSSGGGGSEVQLVESGGIV QPGGSLKLSCAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDDS KNTAYLQMNNLKTEDTAVYCYVRHGNFGNSYISYWAYWGQGLTVTVSSGGGGGGGGGGGSGT

470.	PSMA-9 LH x l2C HL	artificial	nt	VVTQEPSTVSPGGTTLTTCGSSTGAVTSGNYPNWNVQKPGQAPRLIGGKFLAPGTPARFSGS LLGKKAALTILSGVQPEDEAEYYCVLIWYSNRWVFGGTKLTVL AACATCGTGATGACCCAGTCCCAGAAATCATGTCCACCTCTCCCGGGATAGAGTGGCGTGAC CTGCAAGGCCTCCAGAACGTCGGCTCCGACGTGGCTGGTATCAGCCAAAGCCTGGCCAGTCCC CTCGGATCTGTATCTACCTACCTACCTACCGGTACTCCGGCTGCTGACAGATTACCGCTAC GGCTCCGGCACCGACTTCACTGACCTACAAACGTGACGTCGAGTCCGAGGACCTGACCGACTT CTGCCAGCAGTACAACTCCTACCTCTGACCTGGCGTGGCAGTGGCAAGCTGGAACCTGAAGGCG GAGGGGCTCTGGCGGAGGAGAGTGGGGGGGAGTCTCAGGTGACAGTGAAGAGTCCGGC CCTGGCTGTGGCTCTCCAGTCCCTGTCTCATCACTGCACTGTCAGGCTTCCCTGAC CGCTACGGCATCACTGGTGGGCGGAGCTCTGGCAAGGCTGGAATGGCTGGGCTGATCT GGCTGACGGCAACACCGACTACAACAGCACCTGAACTCCGGTGAACATCTTCAAGGACAAC TCCAAGAACAGGTGTTCTGAAGTGTCTTTCAGACCGACGACACCGCCCGGTACTTTG CGCAGGGACTCCTACGGCACTTCAAGGGGCTGTTGATTTTGGGGCCAGGCAACACAC TGACCGTGTCTCCGGAGGTGGTGGATCCGAGGTGAGTGTGAGTCTGGAGGAGGATGGTG CAGCTGGAGGTCAATTGAACTCTCATGTGAGCTCTGGATTCACTTCAATAAGTACGCCAT GAACTGGTCCGCCAGGTCCAGGAAAGGTGGAAATGGTGTGCTGCATAGAAGTAAATATA ATAATTATGCAACATATTATGCCGATTCACTGAAAGACAGGTTACCATCTCCAGAGATTCA AAAAACACTGCCTATCTACAAATGAACACTTGAAACACTGAGGACACTGCCGTGTACTGTGT GAGACATGGAACTTCGGTAAATAGCTACATCTACTGGCTTACTGGGGCCAGGACTCTGG TCACCGTCTCTCAGGTGGTGGTCTGGGGCGGCGCTCCGGTGGTGGTCTCAGACT GTTGTACTCAGGAACCTTCACTACCGTATCACTGGTGAACAGTCACTCACTGTGGCTC CTCGACTGGGCTGTACATCTGGCACTACCAAACTGGTCCAAACAAACAGGTCAGGAC CCGTGGTCTAATAGGTGGACTAAGTCTCCCGGCTGCTCTCCAGATTCTCAGGCTCC CTGCTGGAGGCAAGGTGCTCCCTCACTCAGGGGTACAGGAGGATGAGGACAAATATA CTGTGTTCTATGTTACAGCAACCGCTGGTGTCTGGTGGAGAACCAACTGACTGTCTTA NIVMTQFPKSMISVGERVTLTCKASENVGTYSWYQKPEQSPKMLIYGASNRFTGVDFRTGS GSATDFILTISSVQTEDLVYYCGQSYTFPYTFGGTKLEMK AACATCGTGATGACCCAGTCCCAGTCCATGTCCTCCGTGGGGAGAGAGTACCCTGAC CTGCAAGGCCTCCGAGAACGTCGGCACCTACGTGTCTGGTATCAGCAGAACCTGAGCAGTCCC CTAAGATGTGTATCTACGGCGCTCCAAACAGTTCACCGGCTGCTGACAGATTACCGGCTCC GGCTCCGGCACCGACTTCACTGACCTATCCAGCGTGCAGCCGAGGACCTGGTGGACTACTA CTCGGGCCAGTCTTACCTTCCCTTACCTCCGGGAGGACCAAGCTGGAATGAAG
471.	PSMA-10 VL	artificial	aa	KASENVGTYS GASNRFT
472.	PSMA-10 VL	artificial	nt	EVKLEESGGGLVQPGGSMKLSVASGFTFSNWMNVWRQSPKGLEWVAEIRSQSNFEATHAES VKGRVII SRDDSKSSVYLQMNLRADETGIYCTRRWNFWGQTTLTVSS
473.	PSMA-10 LCDR1	artificial	aa	
474.	PSMA-10 LCDR2	artificial	aa	
475.	PSMA-10 LCDR3	artificial	aa	
476.	PSMA-10 VH	artificial	aa	

477.	PSMA-10 VH	artificial	nt	GAAGTAAAGCTGGAAGAGTCCGGGGAGGACTGGTGCAGCCTGGCGGTCCATGAAGCTGTCCTG CGTGGCTCCGGCTTACCTTCTCAACTACTGGATGAACCTGGTGCAGTCCCTGAGAAAGG GCCTGGAATGGTGGCCGAGATCCGGTCCAGTCCAAACAACTTCGCCACCCACTACGCCGAGTCC GTGAAGGCGAGAGTATCATCTCCGGGAGGACTCCAAAGTCTCCGTGTACCTGCAGATGAACAA CCTCGGGCGGAGGACACCGGCATCTACTACTGACCCCGGGGTGGAACAACTTTTGGGCGCAGG GCACCACACTGACCGTGTCTCTCC
478.	PSMA-10 HCDR1	artificial	aa	NYWMN
479.	PSMA-10 HCDR2	artificial	aa	EIRSQSNNFATHYAESVKG
480.	PSMA-10 HCDR3	artificial	aa	FWNNF
481.	PSMA-10 LH	artificial	aa	NIVMTQFPKSMISVGERVTLTKASENVGTYSWYQQKPEQSPKMLIYGASNRFVTPDRFTGS GSATDFILTISSVQTEDLDVYYCGQSYTFPYTFGGTKLEMKGGGGGGSEVKLEESG GGLVQPGGSMKLSVASGFTFSNYWMNVVRQSPKGLWVAEIRSQSNNFATHYAESVGRVVIS RDSKSSVYLQMNILRAEDTGIYYCTRRNNFWGQGTTLTVSS
482.	PSMA-10 LH	artificial	nt	AACATCGTGATGACCCAGTCCCTAAGTCCATGCTCCGTGGGGAGAGAGTACCCTGAC CTGCAAGGCCTCCGAGAACGTGGGCACCTACGTGTCCTGGTATCAGCAGAAGCCTAGCAGTCCC CTAAGATGCTGATCTACGGCGCTCCACAGGTTACCGGCGTGCCTGACAGATTCACCGGCTCC GGCTCCGCCACCGACTTCATCTGACCATCTCCAGCGTGCAGACCGAGGACCTGGTGACTACTA CTGGCGCAGTCTACACCTTCCCTTACACCTCGCGGAGGACCAAGCTGGAATGAAGGCG GAGGGGATCTGGCGCGAGGAAGTGGAGGGGGCGGATCCGAAGTGAAGCTGGAAGAGTCCGGC GGAGACTGGTGACGCTGGGGCTCCATGAAGTGTCTGCTGGCTTCCGGCTTACCTTCTC CAACTACTGGATGAACCTGGTGCGGCGAGTCCCTGAGAAGGCGCTGGAAATGGGIGCGCGAGATCC GGTCCAGTCCAAACAACTTCGCCACCCACTACCGCGAGTCCGTGAAGGCGAGAGTATCATCTCC CGGACGACTCCAAGTCTCCGTGTACCTGCAGATGAACAACTGGGGCGGAGGACACCGGCAT CTACTACTGACCCGGGTGGAACAACTTTGGGGCGGAGGACCACTGACCGTCTCTCC
483.	PSMA-10 LH x I2C HL	artificial	aa	NIVMTQFPKSMISVGERVTLTKASENVGTYSWYQQKPEQSPKMLIYGASNRFVTPDRFTGS GSATDFILTISSVQTEDLDVYYCGQSYTFPYTFGGTKLEMKGGGGGGSEVKLEESG GGLVQPGGSMKLSVASGFTFSNYWMNVVRQSPKGLWVAEIRSQSNNFATHYAESVGRVVIS RDSKSSVYLQMNILRAEDTGIYYCTRRNNFWGQGTTLTVSSGGGSEVQLVESGGGLVQPGGS LKLSCAASGFTFNKYAMNWRQAPGKGLWVARIRSKYNNIATYYADSVKDRFTISRDDSKNTAY LQMNILKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTTLTVSSGGGSGGGGGGSGQTVVQTE PSLTVSPGGTTLTCCGSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTPARFSGSLIGGK AALTLSGVQPEDEAEYYCVLWYSNRWVFGGTKLTVL
484.	PSMA-10 LH x I2C HL	artificial	nt	AACATCGTGATGACCCAGTCCCTAAGTCCATGTCATCTCCGTGGGGAGAGAGTACCCTGAC CTGCAAGGCCTCCGAGAACGTGGGCACCTACGTGTCCTGGTATCAGCAGAAGCCTGAGCAGTCCC CTAAGATGCTGATCTACGGCGCTCCACAGGTTACCGGCGTGCCTGACAGATTCACCGGCTCC GGCTCCGCCACCGACTTCATCTGACCATCTCCAGCGTGCAGACCGAGGACCTGGTGACTACTA CTGGCGCAGTCTACACCTTCCCTTACACCTCGCGGAGGACCAAGCTGGAATGAAGGCG

				GAGGGGATCTGGCGGAGGAAGTGGAGGGGGGATCCGAAGTGAAGCTGGAAGAGTCCGGC GGAGACTGGTGAGCTGGCGGCTCCATGAAGCTGCTCGTGCTCCGGCTTACCTTCTC CAACTACTGGATGAAGTGGTGCGCCAGTCCCTGAGAAGGCTGGAATGGTGGCGGAGATCC GGTCCAGTCCAACAAGTTCGCCACCCACTAGCCAGTCCGTGAAGGCAGAGTATCATCTCC CGGACGACTCCAAGTCTCGTGTACCTGCAGATGAACAACTGCGGGCCAGGACACCGCAT CTACTACTGACCCCGGTTGAACAACCTTTGGGCCAGGACACACACTGACCGTCTCTCG GAGTGGTGGATCCGAGGTGAGCTGTGATTCACCTTCAATAAGTACGCCATGAAGTGGTCA TTGAAACTCTCATGTGAGCTCTGGATTCAGTTCATGATGAGTGAAGTGAAGTGGTCA GGTCCAGAAAGGTTTGAATGGTGTCTGCATAAAGTAAATATAATATGCAACAT ATTATGCCGATTGAGTGAAGACAGGTTCCACATCTCCAGAGATGATTCAAAAACACTGCCTAT CTACAAATGAACAACCTTGAACACTGAGGACACTGCGGTGTAATACTGTGAGACATGGAACTT CGTAATAGTACATATCTACTGGCTTACTGGGCCAAGGACTGTGTCACCGTCTCTCAG GTGTTGGTGTCTGGCGGCGGCTCCGTGGTGTGTTCTCAGACTGTGACTCAGGAA CCTTCACTACCGTATCACTGGTGAACACTCAGTCACTCACTTGTGGTCTCTCGACTGGGCTGT TACATCTGGCAACTACCCAACTGGGTCCAAACAAAAACAGGTAGGCAACCGTGTCTAATAG GTGGACTAAGTTCCTCGCCCCGGTACTCCTGCCAGATCTCAGGCTCCCTGCTGGAGCAAG GCTGCCCTACCTCTCAGGGTACAGCAGAGATGAGGCAGATATTACTGTGTCTATGGTA CAGCAACCGTGGTGTCTGGTGAAGAACCAACTGACTGTCTTA
485.	PSMA-A VL	artificial	aa	DIQMTQSPSSLSASVDRVTITCRASQGISNYLAWYQQKTKPKFLIYEASTLQSGVPSRFSGG GSGDTFTLTISSLPEDVATYYCQYNNSAPFTFGPTKVDIK
486.	PSMA-A VL	artificial	nt	GACATCCAGATGACCCAGTCCCTCTCTCCCTCTGCTGCTCCGTGGCGACAGAGTACCATCAC CTGCCGGGCTCCAGGGCATCTCCAACACTCTGCTGCTGCTGCTGATCAGCAGAAACCGGCAAGTGC CCAAAGTCTCTGATCTACGAGGCTCCACCTGAGTCCGCGTCCCTTCCAGATTCTCTGGCGGC GGATCCGGCACCGACTTCACCTGACCATCTCCAGCTGAGCCTGAGGACGTGGCCACCTACTA CTGCCAGAACTACAACCTCCGCCCTTTCACCTCGGCCCTGGACCAAGGTGGACATCAAG
487.	PSMA-A LCDR1	artificial	aa	RASQGISNYLA
488.	PSMA-A LCDR2	artificial	aa	EASTLQS
489.	PSMA-A LCDR3	artificial	aa	QYNNSAPFT
490.	PSMA-A VH	artificial	aa	QVQLVSGGTVQPGSRSLRLSCAASGFAFSPRYGMHWVRQAPGKGLEWNAVIWYDGSNKYYADSVK GRFTISRDNKNTQYLOMNSLRAEDTAVYCARGGDFLYYYYYGMDVWGQGTITVSS
491.	PSMA-A VH	artificial	nt	CAGTGCAGCTGGTCGAGTCTGGCGGAGGGTGTGCTCCAGCTGGTCCGCGCTCCCTGAGACTCTCTG CGCCGCTCCGGCTTCGCTTCTCCAGATACGCATCGCTGGTGGCGCAGGCTCCAGCAAGG GACTGGAATGGTGGCGGTGATTGGTACGACGGCTCCAACAAGTACTACGCGGACTCCGTGAAG GGCGGTTCACCATCTCCCGGACAACCTCCAAGAACACCCAGTACCTGAGATGAACCTCCTGAG GGCAGAGGACACCGCGTGTACTACTGGCGCAGAGGGCGGACTTCTGTACTACTATTATACG GCATGACGTGTGGGGCCAGGGCACCCCGTGACAGTGTCTTCC
492.	PSMA-A HCDR1	artificial	aa	RYGMH

493.	PSMA-A HCDR2	artificial	aa	VIWYDGSNKYYADSVKG
494.	PSMA-A HCDR3	artificial	aa	GGDFLYYYGYGMDV
495.	PSMA-A LH	artificial	aa	DIQMTQSPSSLSASVGRVTITCRASQGISNLYAWYQKTKGKPKFLIYEASTLQSGVPSRFSGG GSGTDFTLTISSLQPEDVATYYCQYNAPFTFGPTKVDIKGGSGGGGGQVQLVESG GGVVPGRSLRLSCAASGFAFSGYGMHWVRQAPGKGLEWAVIWDGSKNYADSVKGRFTISR NSKNTQYIQLMNSLRAEDTAVYYCARGGDFLYYYGYMDVWGQGTFTVVS
496.	PSMA-A LH	artificial	nt	GACATCCAGATGACCCAGTCCCTCTCTCCCTGCTCGCTCGTGGGACAGAGTACCATCAC CTGCCGGCCCTCCAGGGCATCTCCAACACTAGTGGCTGGCTGGTATCAGCAGAAACCCGCAAGTGC CCAAGTCTCTGATCTACGAGGCTCCACCTGAGTCCGCTGCTCCAGATTCTCTGGCGG GGATCCGGCACCGACTTCACTGACCATCTCCAGCTGAGCTGAGGACGTGGCCACTACTA CTGCAGAACTACAACTCCGCCCTTTCACCTCGGCCCTGGCACCAAGTGGACATCAAGGGCG GAGGGGAGTGGCGGAGGAGTGGAGGGGGGATCTCAGTGCAGCTGGTGGTGGTGGTGGTGGC GAGGGGTGGTCCAGCTGGCGGTCCCTGAGACTGTCTTGGCGGCTCCGCTTCCGCTTCTC CAGATACGGCATGCACTGGTGGCGGAGTCCAGGCAAGGACTGGAATGGTGGCGGTGATT GGTACGCGCTCCAAACAGTACTACCGGACTCCGTGAAGGCCGTTACCATCTCCCGGAC AACTCCAAGAACACCCAGTACCTGCAGATGAATCCCTGAGGGCAGAGACACCGCGTGTACTA CTGCGCCAGAGGGCGACTTCTCTGTACTACTACTATACGGCATGACGTGTGGGGCAGGGCA CCACCGTGACAGTGTCTTC
497.	PSMA-A LH x I2C HL	artificial	aa	DIQMTQSPSSLSASVGRVTITCRASQGISNLYAWYQKTKGKPKFLIYEASTLQSGVPSRFSGG GSGTDFTLTISSLQPEDVATYYCQYNAPFTFGPTKVDIKGGSGGGGGQVQLVESG GGVVPGRSLRLSCAASGFAFSGYGMHWVRQAPGKGLEWAVIWDGSKNYADSVKGRFTISR NSKNTQYIQLMNSLRAEDTAVYYCARGGDFLYYYGYMDVWGQGTFTVVS LVQPGSLKLSCAASGTFNRYAMNWRQAPGKLEWAVIRSKYNNYATYYADSVKDRFTISR DSKNTAYLQMNHLKTEDTAVYYCVRHGFGNSYISYWAYWGQGLTAVTSSGGSGGGGGSGGS QTVVTQEPSTVSPGGTTLTTCGSGTGAFTSGNYPNWWQKPGQAPRGLIGGTFKFLAPGTPARFS GSLGGKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGTCLTVL
498.	PSMA-A LH x I2C HL	artificial	nt	GACATCCAGATGACCCAGTCCCTCTCTCCCTGCTCGCTCGTGGGACAGAGTACCATCAC CTGCCGGCCCTCCAGGGCATCTCCAACACTAGTGGCTGGCTGGTATCAGCAGAAACCCGCAAGTGC CCAAGTCTCTGATCTACGAGGCTCCACCTGAGTCCGCTGCTCCAGATTCTCTGGCGG GGATCCGGCACCGACTTCACTGACCATCTCCAGCTGAGCTGAGGACGTGGCCACTACTA CTGCAGAACTACAACTCCGCCCTTTCACCTCGGCCCTGGCACCAAGTGGACATCAAGGGCG GAGGGGCGAGTGGCGGAGGAGTGGAGGGGGGATCTCAGTGCAGCTGGTGGTGGTGGTGGC GGAGCGGTGGTCCAGCTGGCGGTCCCTCACTCTCTCGCCCGCTCCGCTTCCGCTTCTC CAGATACGGCATGCACTGGTGGCGGAGTCCAGGCAAGGACTGGAATGGTGGCGGTGATT GGTACGACGGCTCCAAACAGTACTACCGGACTCCGTGAAGGCCGTTACCATCTCCCGGAC AACTCCAAGAACACCCAGTACCTGCAGATGAATCCCTGAGGGCAGAGACACCGCGTGTACTA CTGCCAGAGGGCGACTTCTCTGTACTACTACTATACGGCATGACGTGTGGGGCAGGGCA

				CCACCGTGACAGTGTCTCCGGAGGTGGTGGATCCGAGGTGCAGTGGTGCAGTCTGGAGGAGGA TTGGTGCAGCCTGGAGGTCATTGAACTCTCATGTGCAGCCTCTGGATTCACTTCAATAAGTA CGCCATGAACTGGTCCGCCAGGTCAGGAAAGGTTTGAATTGGTTGCTCGCATTAAGAAGTA AATAATAATTATGCAACATATTATGCCGATTCAAGTGAAGACAGGTTCAACATCTCCAGAGAT GATTCAAAAACACTGCCTATCTACAATGAACAACCTTGAAACTGAGGACACTGCCGTGACTA CTGTGTGAGACATGGGAACCTTCGGTAATAGCTACATATCTACTGGCTTACTGGGGCCAAAGGA CTCTGGTCACCGTCTCCTCAGGTGGTGGTGTCTGGCGCGCGGCTCCGGTGGTGGTGGTCTT CAGACTGTTGACTCAGGAACCTTCACTCACCGTATCACTGGTGAACAGTCACACTCACTTG TGGCTCCTCGACTGGGCTGTACATCTGGCAACTACCAAACTGGTCCAAACAAACAGGTC AGGCACCCCGTGGTCTAATAGGTGGGACTAAGTTCCTCGCCCCGGTACTCCTGCCAGATTCTCA GGTCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGA ATATTACTGTGTCTATGTTACAGCAACCGCTGGGTCTTCGGTGGAGGAACCAAACTGACTGTCC TA
499.	PSMA-B VL	artificial	aa	DIQMTQSPSSLSASVGRVTITCRASQGITNYLAWFQQKPKAPKSLIYAASSLQSGVPSKFSGS GSGTDFSLTISLQPEDFATYYCQQYNSYPITFGQGRLEIK
500.	PSMA-B VL	artificial	nt	GACATCCAGATGACCCAGTACCCCTCCTCCTGTCTGCCTCGTGGCGACAGAGTGACCATCAC CTGCCGGCCTCACAGGCATCAACCACTACCTGGCTGCTTCAGCAGAAAGCTGGCAAGGCC CTAAGTCCCTGATCTACGCCGCTCCTCTCTGCACTCGGCTGCCTTCCAAGTTCTCCGGCTCC GGCTTGGCACCCGACTTCTCCTGACCATCTCCTCCCTGCAGCTGAGGACTTCGCCACCTACTA CTGCCAGCAGTACAACTCCTACCTATCACCTTCGCCAGGCAACCCGGCTGGAATCAAG
501.	PSMA-B LCDR1	artificial	aa	RASQGITNYLA
502.	PSMA-B LCDR2	artificial	aa	AASSLQS
503.	PSMA-B LCDR3	artificial	aa	QQYNSYPIT
504.	PSMA-B VH	artificial	aa	QVQLVESGGGVVQPGRSRLSLCAASGFTFSNVMHWVRQAPKGLEWVAIIWYDGSNKYYADSVK GRFTISRDNKNTLIQMNLSLRAEDTAVYYCAGGYNNWYEHYIGMDVWGQGTITVTVSS
505.	PSMA-B VH	artificial	nt	CAGTGCAGCTGGTCGAGTCTGGCGAGGGTGGTGCAGCCTGGCCGTCCTGAGACTGTCTTG CGCTGCCCTCCGGCTTCACTTCTCAACTACGTGATGCATGGTGGCGCAGGCTCCAGGCAAGG GACTGGAATGGTGGCCATCATTTGGTACGACGGCTCCAACAAGTACTACGCCGACTCCGTGAAG GGCCGGTTCACCATCTCCCGGGACAACCTCCAAGAACACCCCTGTACTCGAGATGAACCTCCCTGAG GGCCGAGGACACCGCCGTGTACTACTGCGTGGCGGCTACAACCTGGAACCTACGAGTACCACTACT ACGGCATGGACGTGTGGGGCCAGGGAACCAACCGTACCGGTGCTCTTC
506.	PSMA-B HCDR1	artificial	aa	NYVMH
507.	PSMA-B HCDR2	artificial	aa	I I WYDGSNKYYADSVKG
508.	PSMA-B HCDR3	artificial	aa	GYNNWYEHYIGMDV
509.	PSMA-B LH	artificial	aa	DIQMTQSPSSLSASVGRVTITCRASQGITNYLAWFQQKPKAPKSLIYAASSLQSGVPSKFSGS GSGTDFSLTISLQPEDFATYYCQQYNSYPITFGQGRLEIKGGGGSGGGSGGGGQVQLVESG

510.	PSMA-B LH	artificial	nt	GGVVPGRSLRLSCAASGTTFSNYMHWVRQAPKGLIEWVAIIWYDGSNKYYADSVKGRFTISRDN NSKNTLYLQMNLSLRAEDTAVYYCAGGYNWNYEHYVMDVWGQGTITVTVSS GACATCCAGATGACCCAGTACCCCTCTCCCTGTCGCTCCGTCGCGCACAGAGTGACCATCAC CTGCCGGCCTCACAGGCATACCAACTACCTGGCCTGGTTCAGCAGAAAGCCTGGCAAGGCC CTAAGTCCCTGATCTACGCCGCTCCTCTCTGAGTCCGGCTGCCTTCCAAGTCTCCGGCTCC GGCTTGGCACCGACTTCTCCCTGACCATCTCTCCCTGACCTGAGGACTTCGCCACTACTA CTGCCAGCAGTACAACTCCTACCTATCACCTTCGGCCAGGACCCGGCTGGAATCAAGGGCG GAGGGGATCTGGCGGAGGAAGTGGAGGGCGGATCTCAGGTGCAGCTGGTCGAGTCTGGC GGAGGGTGGTGCAGCCTGGCCGCTCCCTGAGACTGTCTGGCTGCCTCCGGCTTACCTTCTC CAACTAGTGTGACTGGTGGTGCAGGCTCAGGCAAGGACTGGAATGGTGGCCATCATTT GGTACGACGGCTCCAACAAGTACTAGCCGACTCCGTGAAGGCCGGTTCAACATCTCCGGGAC AACTCCAAGAACACCTGTACCTGCAGATGAATCCCTGAGGCCGAGGACACCGCCCTGTACTA CTGCCCTGGCGCTACAACTGGAACACTACGAGTACCCTACTACGGCATGGACGTGTGGGGCCAGG GAACACCGTGACCGTGTCTTC
511.	PSMA-B LH x I2C HL	artificial	aa	DIQMTQSPSSLSASVGRVTITCRASQGITNYLAWFQKPKAPKSLIYAASSLQSGVPSKFSGS GSGTDFSLT ISSLOPEDFATYYCQYNSYPITFGQGRLEIKGGSGGGSGGGSGVQLVESG GGVVPGRSLRLSCAASGTTFSNYMHWVRQAPKGLIEWVAIIWYDGSNKYYADSVKGRFTISRDN NSKNTLYLQMNLSLRAEDTAVYYCAGGYNWNYEHYVMDVWGQGTITVTVSSGGGSEVQLVESGG GLVQPGSLKLSAASGTFNRYAMNWRQAPKGLIEWVARIRSKYNNYATYYADSVKDRFTISR DDSKNTAYLQMNLLKTEDAVYYCVRHGNFNSYISWAYWGQTLTVTVSSGGSGGGSGGGG SQTIVTQEPSLTVSPGGTTLTCSSTGAVTSGNYPNWWQKPGQAPRGLIIGGTFKFLAPGTPARF SGSLLGKKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGTKLTVL
512.	PSMA-B LH x I2C HL	artificial	nt	GACATCCAGATGACCCAGTACCCCTCTCCCTGTCGCTCCGTCGCGCACAGAGTGACCATCAC CTGCCGGCCTCACAGGCATACCAACTACCTGGCCTGGTTCAGCAGAAAGCCTGGCAAGGCC CTAAGTCCCTGATCTACGCCGCTCCTCTCTGAGTCCGGCTGCCTTCCAAGTCTCCGGCTCC GGCTTGGCACCGACTTCTCCCTGACCATCTCTCCCTGACCTGAGGACTTCGCCACTACTA CTGCCAGCAGTACAACTCCTACCTATCACCTTCGGCCAGGACCCGGCTGGAATCAAGGGCG GAGGGGATCTGGCGGAGGAAGTGGAGGGCGGATCTCAGGTGCAGCTGGTCGAGTCTGGC GGAGGGTGGTGCAGCCTGGCCGCTCCCTGAGACTGTCTTGGCTGCCTCCGGCTTACCTTCTC CAACTAGTGTGCACTGGTGGCCAGGCTCCAGGCAAGGACTGGAATGGTGGCCATCATTT GGTACGACGGCTCCAACAAGTACTACGCCGACTCCGTGAAGGCCGGTTCAACATCTCCGGGAC AACTCCAAGAACACCTGTACCTGCAGATGAATCCCTGAGGGCCGAGGACACCGCCGTGTACTA CTGGCTGGCGGCTACAACTGGAACACTACGAGTACCCTACTACGGCATGGACGTGTGGGGCCAGG GAACACCGTGACCGTGTCTTCCGAGGTGGTGAATCCGAGGTGCAGCTGGTCGAGTCTGGAGGA GGATTGGTGCAGCCTGGAGGTGATTGAACTCATGTGCAGCCTCTGGATTCACTTCAATAA GTACGCCATGAACGTGGTCCGCCAGGCTCCAGGAAAGGGTTTGGAAATGGGTGCTCGCATAGAA GTAATAATAATAATTATGCAACATATTATGCCGATTTCAGTGAAGACAGGTTTCAACATCTCCAGA

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525.	PSMA-C LH x 12C HL	artificial	aa	<p>CTAAGTCCCTGATCTACGGCCGCTCCTCTCTGAGTCCGGCTGCTTCCAAGTTCTCCGGTCC GGCTCTGGCACCGACTTCAACCTGACCATCTCCAGCTGCAGCTGAGGACTTCGCCCTACTACTA CTGCCAGCAGTACAACCTCTCTCTGACCTTCGGCGGAGGACCAAGTGGAGATCAAGGCG GAGGGCTCTGGCGGAGGAGTGGAGGGGGGATCTCAGGTGACGTGGTTCGAGTCTGGC GGAGGGTGGTGCAGCTGGCCGCTCCCTGAGCTCTTGTCCGCTCCGGCTTACCTTCTC CTCTACGGCATGCACTGGGTGCCAGGCTCCAGGCAAGGACTGAGTGGTGGCCATCATCT GGCAGACGGCTCCAACAAGTACTACGCCGACTCCGTGAAGGCCGCTTACCATCTCCGGGAC AACTCCAAGAAAACCTGTACCTGCAGTGAATCCCTGAGGCCGAGGACACCGCCGTGTACTA CTGTGCCAGGGCTGGCCCTACGACTACGGCACTACGAGTACTACTTCCGCACTGGACGTGGG GCCAGGGCACCGGTGACAGTGTCTC</p>
526.	PSMA-C LH x 12C HL	artificial	nt	<p>DIQMTQSPSSLSASVGDRVTITCRASQGISHYLAWFQKPKAPKSLIYAASSLQSGVPSKFSGS GSGTDFLTITSSLPEDFATYYCQQYNFPLTFGGTKVEIKGGSGGGGGGGGQVLVESG GGVQPGRSRLSCAASGFTFSSYGMHWVRQAPKGLDVAIIWHDGSNKYYADSVKGRFTISR NSKKTLYLQMNLSRAEDTAVYYCARAWYDYGDYEEYFGMDVWGQTTVTYVSSGGGSEVQLVES GGGLVQPGGSLKLSCAASGFTENKYAMNWRQAPKGLSEWVARIRSKYNNYATYYADSVKDRFTI SRDDSKNTAYLQMNLLKTEDTAVYYCVRHGNFNSYISYWAYWGQTLTVTVSSGGGSGGGSGG GGSQTVVVTQEPSLTVSPGGTTLTCGSSSTGAVTSGNYPNVQKPGQAPRGLIGGTRKFLAPGTPA RFGSLLGGKAAITLSGVQPEDEAEYVCILWYSNRWVFGGTKLTVL</p>

					ACTACTGTGGTCTCTCGACTGGGCTGTTACATGTGCAACTACCAAACTGGTCCAAACAAA AACCAGGTACGGACACCCGCTGGTCTAATAGGTGGACTAAGTCTCTCGCCCCGGTACTCCTGCC AGATTCTCAGGCTCCCTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCACAGGA TGAGGCAGAAATATTACTGTGTTCTAAGTACACCAACCGCTGGTGTTCGGTGGAGGAACCAAC TGACTGTCCTA
527.	PSMA-D VL	artificial	aa		GIVMTQSPATLSVSPGERATLSCRTSQSIGWNLAWYQQKPGQAPRLIIYGASSRTTGIPIARFSGS GSGTEFTLTISLQSEDSAVYYQCQHYDNWPMCSFGQGTELEIK
528.	PSMA-D VL	artificial	nt		GGCATCGTGATGACCCAGTCCCCCGCCACCCTGTCTGTGTCTCCCGCGAGAGAGCCACCTGAG CTGCCGACCTCCAGTCCATCGGCTGGAACTGGCTGGTATCAGCAGAACCTGGACAGGCC CTAGACTGCTGATCTACGGGCTCTCTCCAGAACACCGGCATCCCTGCCAGGTTCTCCGGCTCT GGTCCGGCACCGAGTTCACCTGACCATCTCCAGCTCCAGCTCCGAGGACTCCGCCGTGCTACTA CTGCCAGCACTACGACAACTGGCCTATGTCTCTCGCCAGGCCACCGAGCTGGAATCAAG
529.	PSMA-D LCDR1	artificial	aa		RTSQSIGWNLA
530.	PSMA-D LCDR2	artificial	aa		GASRTT
531.	PSMA-D LCDR3	artificial	aa		QHYDNWPMCS
532.	PSMA-D VH	artificial	aa		EVQLVQSGAEVKKPESLKISKCKSGSYFTSYWIGVVRQMPKGLWGMGIIYPGDSDTRYSPSFQ GQVTISADKSI STAYLQWSSLKASDTAMYICARRMAAAGPFDYWGQGLTVTVSS
533.	PSMA-D VH	artificial	nt		GAAGTCAGTGTGGTGCAGTCTGGCGCGAAGTGAAGAAGCCCGGCGAGTCCCTGAAGATCTCTG CAAGGCTCCGGCTACTCTCTACCTCCTACTGATCGGCTGGTGGCCAGATGCCGTGGAAGG GCTGGAATGGATGGCATCATCTACCTGGGACTCCGACACCCGCTACTCTCCAGCTTCCAG GGCAGGTGACCATCTCTGCCGACAAGTCCATCTCCACCGCTACCTGCAGTGGTCTCCCTGAA GGCTCCGACACCGCCATGTACTATTGGCCAGCGGATGGCCGCTGCCGGCCCTTTTGATTACT GGGGCAGGGAACCTGGTGACCGTGCTCTCC
534.	PSMA-D HCDR1	artificial	aa		SYWIG
535.	PSMA-D HCDR2	artificial	aa		I IYPGDSDTRYSPSFQ
536.	PSMA-D HCDR3	artificial	aa		RMAAAGPFDY
537.	PSMA-D LH	artificial	aa		GIVMTQSPATLSVSPGERATLSCRTSQSIGWNLAWYQQKPGQAPRLIIYGASSRTTGIPIARFSGS GSGTEFTLTISLQSEDSAVYYQCQHYDNWPMCSFGQGTELEIKGGGGGGGGGGSEVQLVQS GAEVKKPESLKISKCKSGSYFTSYWIGVVRQMPKGLWGMGIIYPGDSDTRYSPSFQGVITISA DKSI STAYLQWSSLKASDTAMYICARRMAAAGPFDYWGQGLTVTVSS
538.	PSMA-D LH	artificial	nt		GGCATCGTGATGACCCAGTCCCCCGCCACCCTGTCTGTCTCTCCCGCGAGAGAGCCACCTGAG CTGCCGACCTCCAGTCCATCGGCTGGAACCTGGCTGGTATCAGCAGAACCTGGACAGGCC CTAGACTGCTGATCTACGGGCTCTCTCCAGAACACCGGCATCCCTGCCAGGTTCTCCGGCTCT GGTCCGGCACCGAGTTCACCTGACCATCTCCAGCTGCAGTCCGAGGACTCCGCCGTGCTACTA CTGCCAGCACTACGACAACTGGCCTATGTCTCTCGCCAGGCCACCGAGCTGGAATCAAGG GCGAGGGGGATCTGGCGCGGAGGAAGTGAGGGGGGGCGGATCCGAAGTGCAGCTGGTGCAGTCT

<p>GGGCGGAAGTGAAGAACCCGGGAGTCCCTGAAGATCTCTGCAAGGCTCCGGCTACTCCTT CACCTCCTACTGGATCGGCTGGGTGGCCAGATCGCTGGCAAGGCTGGAATGGATGGCATCA TCTACCTGGGACTCCGACACCCGGTACTCTCCAGCTTCCAGGCCAGGTGACCATCTTGCC GAAAGTCCATCTCCACCGCTACCTGCAGTGGTCCCTGAAGCCTCCGACACCGCATGTA CTATGCGCCAGCGGATGCGCGCTGCCGCCCTTTGATTACTGGGCCAGGGAACCCGGTGA CCGTGCTCTCC</p>				<p>GIWMTQSPATLSVSPGERATLSCRTSQSIGWNLAWYQKPGQAPRLIYGASSRTTGIPARFSGS GSSEFTLTISLQSEDSAVYYCQHYDNWPMCSFGQTELEIKGGSGGGGGGGSEVQLIVQS GAEVKPGESLKISCKGSGYSFTSYWIGWRQMPKGLEWMGIYPGDSDTRYSPSFQGVITISA DKSISTAYLQWSSLKASDTAMYICARRMAAGPFDYWGQGLTVTVSSGGGSEVQLVESGGGLVQ PGGSLKLSCAASGFTENKYAMNWVRQAPGKLEWVARIRSKYNNYATYYADSVKDRFTISRDSK NTAYLQMNNLKTEDAVYYCVRHGNFNSYISYWAYWGQGLTVTVSSGGGSGGGSGGSQTV VTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWQKPGQAPRLIGGTFKFLAPGTPARFSGSL LGKKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGGLTIVL</p>
<p>539. PSMA-D LH x I2C HL</p>	<p>aa</p>	<p>artificial</p>		<p>GGCATCGTGATGACCCAGTCCCCCGCCACCTCTGTCTCTCCGGCGAGAGAGCCACCTGAG CTGCGGACCTCCAGTCCATCGGCTGGAACTTGGCTGGTATCAGCAGAGCCCTGGACAGGCC CTAGACTGCTGATCTACGGGCTCTCTCCAGAACACCGGCATCCCTGCCAGTTCTCCGGCTCT GGCTCCGGCACCGAGTTACCCCTGACCATCTCAGCTGCAGTCCGAGGACTCCGCCGCTACTA CTGCCAGCACTACGACAACTGGCCTATGTCTCTCGCCAGGACCCAGCTGGAATCAAGG GCGAGGGGATCTGGCGGGGAGGAAGTGAAGGGGGGATCCGAACTGAGCTGGTGCAGTCT GGCGCGAAGTGAAGAACCCGGGAGTCCCTGAAATCTCTCAAGGCTCCGGCTACTCCTT CACCTCCTACTGGATCGGCTGGTGGCCAGATCCCTGGCAAGGCCCTGGAATGGATGGGCATCA TCTACCTTGGGACTCCGACACCCGGTACTCTCCAGCTTCCAGGCCAGGTGACCATCTTGCC GACAACTCCATCTCCACCGCTACCTGCAGTGGTCTCCCTGAAGGCTCCGACACCGCATGTA CTATTGCGCCAGCGGATGGCGCTGCCGCCCTTTGATTACTGGGCCAGGGAACCTGGTGA CCGTGCTCTCCGAGGTGGTGGATCCGAGTGCAGTGGTGGTGCAGTCTGGAGGAGTGGTGCAG CTGGAGGTCTATTGAACTCTCATGTGACGCTCTGGATTCACTTCAATAAGTACGCCATGAA CTGGTCCGCCAGGCTCCAGCAAGGTTTGAATGGTTGCTCGCATAGAAGTAATAATA ATTATGCAACATATTATGCCGATTTCAGTGAAGACAGGTTACCATCTCCAGAGATGATCAAAA AACACTGCCCTATTACAAATGAACAACTTGAATGAGGACACTGCCGTGACTACTGTGTGAG ACATGGGAACCTCGGTAATAGTACATATCCACTGGGCTTACTGGGCCAAGGACTCTGGTCA CCCTCTCTCAGTGGTGGTGGTCTTGGCGGGCGGCTCCGGTGGTGGTCTCAGACTGT GTGACTCAGGAACCTTCACTCACCGTATCACCTGGTGGAAACAGTCACTCACTTGTGGTCTCTC GACTGGGCTGTACATCTGGCAACTACCCAACTGGGTCCAAACAAACAGGTCAAGGACCCC GTGGTCTAATAGGTGGACTAAGTCTCTCGCCCCGGTACTCTCTCCAGATTCTCAGGCTCCCTG CTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGGATGAGGCAGATATATCTG TGTTCTATGTTACAGCAACCGCTGGGTGTTCTGGTGGAGAACCAACTGACTGTCTTA</p>
<p>540. PSMA-D LH x I2C HL</p>		<p>artificial</p>	<p>nt</p>	

541.	PSMA-E VL	artificial	aa	DIVMTQTPLSLSVTPGQPASISCKSSQSLHSDGKTFLYWYLOKPGQPPQLLIYEVSNRFSGVDP RFGSGSGTDFTLKISRVEAEDVGLYYCMQSIQLPLTFGGGKVEIK
542.	PSMA-E VL	artificial	nt	GACATCGTGATGACCCAGACCCCTCTGTCCCTGTGTGACCCCTGGCCAGCCTGCCTCATCTC CTGCAAGTCTCTCCAGTCCCTGCTGCACTCCGACGGCAAGACCTTCTGTACTGTATCTGCAGA AGCCCGCCAGCCTCCTCAGCTGCTGATCTACGAGGTGTCCAAACCGGTTCTCCGGCGTGCTGAC AGGTCTCTGGCTCCGGCTCCGGCACCGACTTCCCTGAAGATCTCCCGGTGGAGGCTGAGGA CGTGGCCTGTACTACTGCATGCAGTCCATCCAGCTGCCTCTGACCTTCGGCGGAGGACCAAGG TGGAGATCAAG
543.	PSMA-E LCDR1	artificial	aa	KSSQSLHSDGKTFLY
544.	PSMA-E LCDR2	artificial	aa	EVSNRF
545.	PSMA-E LCDR3	artificial	aa	MQSIQLPLT
546.	PSMA-E VH	artificial	aa	QVQLVESGGGVQPGRSRLRLSCAASGFTFISYGMHWRQAPGKGLEWAVISYDGSNKYYADSVK GRETIIRDNSKNTLYLQMNLSRAEDTAVYICARVLVYALYYNYGMVWGQTTVTVSS
547.	PSMA-E VH	artificial	nt	CAGGTGAGCTGGTCGAGTCTGGGGAGGGGTCTGCAGCCTGCCGCTCCCTGAGACTGTCTTG CGCGCCTCCGGCTTCACTTCTTACGGCATGCACTGGTGCGCCAGGCTCCAGGCAAGG GACTGAATGGTGGCGGTGATCTCTACGACGGTCCAACAAGTACTACGCCGACTCCGTGAAG GGCGGTACCATCTCCCGGACAACTCCAAGAACCCTGTACTGCAGATGAATCCCTGAG GGCCGAGGACACCGCGTGTACTACTGTGCCAGGCTGTGGCGCTCTGTACTACTAACT ACTACGGCATGACGTGTGGGGCCAGGGCAACCGTGACAGTGTCTTCC
548.	PSMA-E HCDR1	artificial	aa	SYGMH
549.	PSMA-E HCDR2	artificial	aa	VISYDGSNKYYADSVKG
550.	PSMA-E HCDR3	artificial	aa	VIVGALYYNYGMV
551.	PSMA-E LH	artificial	aa	DIVMTQTPLSLSVTPGQPASISCKSSQSLHSDGKTFLYWYLOKPGQPPQLLIYEVSNRFSGVDP RFGSGSGTDFTLKISRVEAEDVGLYYCMQSIQLPLTFGGGKVEIKGGGSGGGSGGGGQVQ LVESGGGVQPGRSRLRLSCAASGFTFISYGMHWRQAPGKGLEWAVISYDGSNKYYADSVKGRF TISRDNKNTLYLQMNLSRAEDTAVYICARVLVYALYYNYGMVWGQTTVTVSS
552.	PSMA-E LH	artificial	nt	GACATCGTGATGACCCAGACCCCTCTGTCCCTGTGTGACCCCTGGCCAGCCTGCCTCATCTC CTGCAAGTCTCTCCAGTCCCTGCTGCACTCCGACGGCAAGACCTTCTGTACTGTATCTGCAGA AGCCCGCCAGCCTCCTCAGCTGTGATCTACGAGGTGTCCAAACCGGTTCTCCGGCGTCCCTGAC AGGTCTCTGGCTCCGGCTCCGGCACCGACTTCACTTGAAGATCTCCCGGTGGAGGCTGAGGA CGTGGCCTGTACTACTGCATGCAGTCCATCCAGTCCCTCTGACCTTCGGCGGAGGACCAAGG TGGAGATCAAGGGCGGAGGGGCTCTGGCGGAGGAGGAGTGGAGGGGCGGATCTCAGGTGCAG CTGTCTCAGTCTGGGGAGGGGTCTGTGAGCTGCGCGGTCTCTGAGACTGTCTTGGCGGCTC CGGCTTCACTTCACTCTTACGGCATGCATGGGTGGCCAGGCTCCAGGCAAGGCTGGAAT GGGTGGCGGTGATCTCTACGACGGTCCAACAAGTACTACGGGCTCCGTGAAGGGCCGTTTC ACCATCTCCCGGACAACTCCAAGAACACCCCTGTACTGCAGATGAATCCCTGAGGGCCGAGGA

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				CTGCCGGCCCTCCAGGGCATCTCTTCGGCCCTGGCTGGTATCAGCAGAAAGTCCGGCAAGGCC CTAAGCTGTGATCTTCGACGCCCTCCTCTGGAATCCGGCTGCCTCCGGTCTCCGGCTCT GGCTCCGGCACCAGACTTCAACCTGACCATCTCCAGCCTGCAGCTGAGGACTTCGCCACCTACTA CTGCACGAGTTCAACTCCTACCTCTGACCTTCGGCGGAGGACCAAGGTGGAGATCAAG
557.	PSMA-F LCDR1	artificial	aa	RAQQISSALA
558.	PSMA-F LCDR2	artificial	aa	DASSLES
559.	PSMA-F LCDR3	artificial	aa	QQENSYPILT
560.	PSMA-F VH	artificial	aa	QVQLVESGGGVQPGPGRSLRLSCAASGFTFSYAMHWVRQAPGKLEWAVISYDGNKYYADSVK GRETI SRD NSKNTLY LQMNSLRAEDTAVYCARAVPWGSRYYYGMQDVGQTTVTVSS
561.	PSMA-F VH	artificial	nt	CAGGTGAGCTGGTCGAGTCTGGGGAGGGTCTGTGAGCCTGGCCGTCCTGAGACTGTCTTG CGCCGCTCCGGCTTCACTTCTCCTTACCCATGCATGGTGGCCAGGCTCCAGCAAGG GACTGGAATGGTGGCGGTGATCTCTACGACGGCAACAAGTACTACGCCGACTCCGTGAAG GGCCGTTCAACATCTCCGGGACAACCTCAAGAACACCTGTACCTGCAGATGACTCCCTGAG GGCTGAGGACACCGCCGTGTACTACTGCGCCAGAGCCGTGCTTGGGCTCCCGGTACTACT ACGGCATGGACGTGTGGGGCCAGGGCACCAAGTGTCTTTC
562.	PSMA-F HCDR1	artificial	aa	SYAMH
563.	PSMA-F HCDR2	artificial	aa	VISYDGNKYYADSVKG
564.	PSMA-F HCDR3	artificial	aa	AVPWGSRYYYGMQD
565.	PSMA-F LH	artificial	aa	AIQLTQSPSSLSASVDRVTITCRASQGISSALAWYQQKSGKAPKLLIFDASSLESVPSRPSGS SGTDFTLTISLQPEDFATYYCQNFNSYPLTFGGGTKEIKGGSGGGGGSGVQLVESG GGVQPGPGRSLRLSCAASGFTFSYAMHWVRQAPGKLEWAVISYDGNKYYADSVKGRFTISR NSKNTLY LQMNSLRAEDTAVYCARAVPWGSRYYYGMQDVGQTTVTVSS
566.	PSMA-F LH	artificial	nt	GCCATCCAGCTGACCCAGAGTCCCTCCTCTGCTGCTCCGTGGGGCAGAGTGACCATCAC CTGCCGGCCCTCCAGGGCATCTCTTCGGCCCTGGCTGTATCAGCAGAAAGTCCGGCAAGGCC CTAAGCTGTGATCTTCGACGCCCTCCTCTGGAATCCGGCTGCCTCCGGTCTCCGGCTCT GGTCCGGCACCGACTTCACTCCTGACCTTCCAGCCTGCAGCCTGAGGACTTCGCCACTACTA CTGCCAGAGTTCAACTCCTACCTGTACCTTCGGGGAGGACCAAGTGGAGATCAAGGCGG CAGGGGCTCTGGGGCGGAGGAGTGGAGGGGGGATCTCAGTGCAGCTGGTCGAGTCTGGG GGAGGGTCTGCAGCCTGGCCGGTCCCTGAGACTGTCTTGGCCGCTCCGGCTTCACTCTC CTCTTACGCCATGCACTGGTGGCCAGGCTCAGGCAAGGACTGGAATGGTGGCCGCTGATCT CCTACGACGGCAACAACAAGTACTACCGGACTCCGTGAAGGCCGTTCAACATCTCCCGGAC AACTCCAAGAACACCCGTGTACCTGCAGATCACTCCTGAGGGCTGAGGACACCGCCGTACTA CTGCCAGAGAGCCGTGCCTTGGGGCTCCCGGTACTACTACGGCATGGACGTGTGGGGCCAGG GCACACCGTGACAGTCTTCC
567.	PSMA-F LH x I2C HL	artificial	aa	AIQLTQSPSSLSASVDRVTITCRASQGISSALAWYQQKSGKAPKLLIFDASSLESVPSRPSGS SGTDFTLTISLQPEDFATYYCQNFNSYPLTFGGGTKEIKGGSGGGGGSGVQLVESG

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571.	PSMA-J LCDR1	artificial	aa	RAQSQSVSSYLA
572.	PSMA-J LCDR2	artificial	aa	DASNRA ^T
573.	PSMA-J LCDR3	artificial	aa	QQRSNWL ^{MY} T
574.	PSMA-J VH	artificial	aa	EVQIVQSGAEVKKPGESLKISCKGSGYSTSYWIGWARQMPKGLEWMGIIYPGSDSTRYSPSFQ GQVTISADKSIISTAYLQWSSLKASDTAMYCYSAANSSHWFYDLWGRGTLTVSS
575.	PSMA-J VH	artificial	nt	GAAGTGCAGCTGGTGCACTCTGGGCGCGAAGTGAAGACCCGGCGAGTCCCTGAAGATCTCTCTG CAAGGGCTCCGGGTACTCTTCACTCTCTGATCGGCTGGCCAGGAGATGCCAGGCAAGG GCCTGGAATGGATGGGCATCATCTACCTGGGACTCCGACACCCGGTACTCTCCAGCTTCCAG GGCAGGTGACCATCTCTGCCGACAAGTCCATCTCCACGCCCTACCTGCAGTGGTCTCCCTGAA GGCTCCGACACCGCCATGTACTATTGCTCCGCGCCAACTCTCCCACTGGTACTCGACCTGT GGGCAGAGCACCTGGTGACCGTGCTCTCC
576.	PSMA-J HCDR1	artificial	aa	SYWIG
577.	PSMA-J HCDR2	artificial	aa	IYPGSDSTRYSPSFQ
578.	PSMA-J HCDR3	artificial	aa	ANSSHWFYDL
579.	PSMA-J LH	artificial	aa	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWFQQKPGQAPRLLIYDASNRATGIPARFSGS GSGTDFTLTISLLEPEDFAVYYCQQRNWL ^{MY} TFGQTKLEIKGGGSGGGSGGGSEVQLVQS GAEVKKPGESLKISCKGSGYSTSYWIGWARQMPKGLEWMGIIYPGSDSTRYSPFQGVQVTISA DKSISTAYLQWSSLKASDTAMYCYSAANSSHWFYDLWGRGTLTVSS
580.	PSMA-J LH	artificial	nt	GAGATCGTGTGACCCAGTCCCTGCCACCTGTCTCTGTCTCCCGGAGAGACCCCTGAG CTGCCGGCCTCCAGTCCGTCTCTCTACCTGGCTGGCTGGTCCAGCAGAACCTGGACAGGCC CTAGGTGTGTATCTACGACGCTCCAAAGGGCTACCGGCATCCCTGCCGGTCTCCGGCTCT GGCTCCGGCACCGACTTCACTGACCATCTCCAGCTGGAACCTGAGGACTTCGCCGTGTACTA CTGCCAGACGGTCCAACTGGCTGATGATATACCTTCGGCCAGGCAACCAAGCTGGAATCAAGG GCGAGGGGGATCTGGGGCGGAGGAGTGGAGGGGGCGGATCCGAAGTGCAGCTGGTGCAGTCT GGCCCGAAGTGAAGAACCCCGGAGTCCCTGAAGATCTCTGCAAGGCTCCGGGTACTCCTT CACCTCCTACTGGATCGGTGGCCAGGAGATGCCAGGCAAGGCCCTGGAATGGATGGCATCA TCTACCTGGCGACTCCGACACCCGTA ^T CTCTCCAGCTTCAGGGCCAGGTGACCATCTCTGCC GACAAGTCCATCTCCACCGCTACCTGCAGTGGTCTCTCTGAAGGCCCTCCGACACCGCATGTA CTATTGCTCCGGCGCAACTCCTCCACTGGTACTCTGACCTGTGGGCGAGAGGACCCCTGGTGA CCGTGCTCTCC
581.	PSMA-J LH x I2C HL	artificial	aa	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWFQQKPGQAPRLLIYDASNRATGIPARFSGS GSGTDFTLTISLLEPEDFAVYYCQQRNWL ^{MY} TFGQTKLEIKGGGSGGGSGGGSEVQLVQS GAEVKKPGESLKISCKGSGYSTSYWIGWARQMPKGLEWMGIIYPGSDSTRYSPFQGVQVTISA DKSISTAYLQWSSLKASDTAMYCYSAANSSHWFYDLWGRGTLTVSSGGGSEVQLVESGGGLVQ PGGSLKLSCAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYYADSVKDRFTISRDDSK NTAYLQMN ^N LKTEDTAVYYCVRHGFNGNSYISYWAYWGQGT ^L TVSSGGGSGGGSGGGGSGQTV

52.	PSMA-J LH x 12C HL	artificial	nt	<p>VTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTFPARESGSL LGGKAALTISGVQPEDEAEYICVLWYSNRWVFGGTFKLTVL</p> <p>GAGATCGTCTGACCCAGTCCCTGCCACCCCTGTCTGTCTCCCGGCGAGAGAGCCACCCCTGAG CTCGGGGCTCCAGTCCGTGTCTCTCTACCTGGCTGGTTCAGCAGAGCCCTGGACAGGCC CTAGGCTGTGATCTACGACGCCCTCCACAGGGGTACCGGCATCCCTGCCGGTTCCTCCGGCTCT GGTCCGGCACCGACTTCACTGCTGATGTATACCTCCAGCTTCCAGCTGAGGACTTCGCCGTGTA CTGCCAGCAGCGGTCCAACTGGCTGATGTATACCTTCGGCCAGGACCAAGCTGGAATCAAGG GCGGAGGGGATCTGGGGCGGAGGAGTGGGGGGGGGATCCGAAAGTGCAGCTGGTGCAGTCT GGCGGAAAGTGAAGAACCCGGCGAGTCCCTGAAGATCTCTCAAGGCTCCGGGTACTCTCT CACCTCTACTGGATCGGCTGGCCAGGAGATGCCAGGCAAGGCCCTGGAATGGATGGCATCA TCTACCTGGGACTCCGACACCCGGTACTCTCCAGCTTCAGGCGCAGGTGACCATCTCTGCC GACAGTCCATCTCCACGCCCTACCTGCAGTGGTCTCCCTGAAGCCTCCGACCCGCCATGTA CTATTGCTCCGGCCCACTCTCCACTGGTACTTCGACCTGTGGGCGAGGACCCCTGGTGA CCGTGCTTCGGAGGTGGTGGATCCGAGGTGCAGTGGTGCAGTCTGGAGGAGGATTGGTGCAG CCTGGAGGCTATTGAACTCTCATGTGCAGCTCTGGATTCACTTCAATAAGTACGCCATGAA CTGGTCCGCCAGGCTCCAGGAAAGGTTTGGATGGTGTCTGCATAAGAAATAATAATA ATTATGCAACATATTATGCCGATTGAGTGAAGACAGGTTTCACTATCCAGAGATGATTCAAAA AACACTGCCCTATCTACAAATGAACAACTTGAATACTGAGGACACTGCCGTGTACTGTGTGAG ACATGGAACTTCGGTAATAGTACATATCTTACTGGCTTACTGGGCGCAAGGACTCTGGTCA CCGTCTCTCAGGTGGTGGTGTCTGGCGGGCGGCTCCGGTGGTGGTGTCTCAGACTGTT GTGACTCAGGAACCTTCACTACCGTATCACTGGTGGACAGTCACTCACTTGTGGTCTCTC GACTGGGCTGTATACATCTGGCAACTACCCAACTGGGTCCAAACAAACAGGTCAGGCAACCC GTGCTAATAGGTGGGACTAAGTCTCTCGCCCGGCTACTCTGCCAGATTCTCAGGCTCCCTG CTTGAGGCAAGGTGCCCTCACTCTCAGGGGTACAGCCAGAGGATGAGGCAAGATATTA TGTTCTATGCTACAGCAACCGCTGGTGTTCGGTGGAGGAAACCAACTGACTGTCTTA</p>
583.	PSMA-L VL	artificial	aa	<p>EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRAIGIPARFSGS GSGTDFLTLSLEPEDFAVYYCQQRSQDWLMTFGQGTKEIK</p>
584.	PSMA-L VL	artificial	nt	<p>GAGATCGTCTGACCCAGTCCCTGCCACCCCTGTCTCTCCCGGCGAGAGAGCCACCCCTGAG CTCGGGGCTCCAGTCCGTGTCTCTCTACCTGGCTGGTATCAGCAGAGCCCTGGACAGGCC CTAGGCTGTGATCTACGACGCCCTCCACAGGGGTACCGGCATCCCTGCCGGTTCCTCCGGCTCT GGTCCGGCACCGACTTCACTGCTGATGTATACCTTCGGCCAGGACCAAGCTGGAATCAAGG CTGCCAGCAGCGGTCCAACTGGCTGATGTATACCTTCGGCCAGGACCAAGCTGGAATCAAGG GCGGAGGGGATCTGGGGCGGAGGAGTGGGGGGGGGATCCGAAAGTGCAGCTGGTGCAGTCT GGCGGAAAGTGAAGAACCCGGCGAGTCCCTGAAGATCTCTCAAGGCTCCGGGTACTCTCT CACCTCTACTGGATCGGCTGGCCAGGAGATGCCAGGCAAGGCCCTGGAATGGATGGCATCA TCTACCTGGGACTCCGACACCCGGTACTCTCCAGCTTCAGGCGCAGGTGACCATCTCTGCC GACAGTCCATCTCCACGCCCTACCTGCAGTGGTCTCCCTGAAGCCTCCGACCCGCCATGTA CTATTGCTCCGGCCCACTCTCCACTGGTACTTCGACCTGTGGGCGAGGACCCCTGGTGA CCGTGCTTCGGAGGTGGTGGATCCGAGGTGCAGTGGTGCAGTCTGGAGGAGGATTGGTGCAG CCTGGAGGCTATTGAACTCTCATGTGCAGCTCTGGATTCACTTCAATAAGTACGCCATGAA CTGGTCCGCCAGGCTCCAGGAAAGGTTTGGATGGTGTCTGCATAAGAAATAATAATA ATTATGCAACATATTATGCCGATTGAGTGAAGACAGGTTTCACTATCCAGAGATGATTCAAAA AACACTGCCCTATCTACAAATGAACAACTTGAATACTGAGGACACTGCCGTGTACTGTGTGAG ACATGGAACTTCGGTAATAGTACATATCTTACTGGCTTACTGGGCGCAAGGACTCTGGTCA CCGTCTCTCAGGTGGTGGTGTCTGGCGGGCGGCTCCGGTGGTGGTGTCTCAGACTGTT GTGACTCAGGAACCTTCACTACCGTATCACTGGTGGACAGTCACTCACTTGTGGTCTCTC GACTGGGCTGTATACATCTGGCAACTACCCAACTGGGTCCAAACAAACAGGTCAGGCAACCC GTGCTAATAGGTGGGACTAAGTCTCTCGCCCGGCTACTCTGCCAGATTCTCAGGCTCCCTG CTTGAGGCAAGGTGCCCTCACTCTCAGGGGTACAGCCAGAGGATGAGGCAAGATATTA TGTTCTATGCTACAGCAACCGCTGGTGTTCGGTGGAGGAAACCAACTGACTGTCTTA</p>
585.	PSMA-L LCDR1	artificial	aa	RASQSVSSYLA
586.	PSMA-L LCDR2	artificial	aa	DASNRAI
587.	PSMA-L LCDR3	artificial	aa	QQRSQDWLMT
588.	PSMA-L VH	artificial	aa	<p>EVQLVQSGAEVKTPEGESLISKCKGSGYFTTSYWIQWVQMPGKGPPEWMGIIPGDSDFRISPSFQ GQVTFSDAKSISTAYLIQWNSLKTSDTAMYICATNPSYWFYDLWGRGTLTVSS</p>

589.	PSMA-L VH	artificial	nt	GAATGTCAGCTGGTGCAGTCTGGCGCGAAGTGAACCCCTGGCGAGTCCCTGAAGATCTCCTG CAAGGCTCCGGCTACACCTTACCTCTTACTGATCGGTGGTGGCCAGATGCCCTGGCAAGG GCCCTGAGTGGATGGCATCATACCTGGGACTCCGACACCCGGTACTCTCCAGTCCAG GGCAGGTGACCTTCTCCGCGGACAACTCCATCTCCACCGCTACCTGAGTGAACCTCCTGAA AACCTCCGACACCGCATGTACTATTGGCGCACCGCCAAACCTAGCTACTGGTACTTCGACCTGT GGGCAGAGGCACCTGGTGACCGTGCTTCC
590.	PSMA-L HCDR1	artificial	aa	SYWIG
591.	PSMA-L HCDR2	artificial	aa	I IYPGDS DTRYSPSFQG
592.	PSMA-L HCDR3	artificial	aa	ANPSYWFDL
593.	PSMA-L LH	artificial	aa	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRAIGIPARFSGS GSGTDFTLTISSLEPEDFAVYQCQRSDWLMYTFGQGTKLEIKGGGGSGGGGGSEVQLIVQS GAEVKTPGESLKISCKSGSYTFTSYWIGWVRQMPGKGPPEWMGI IYPGDS DTRYSPSFQGVTFSA DKSISTAYLQWNSLKTSDTAMYCATANPSYWFDLWGRGTLIVTSS
594.	PSMA-L LH	artificial	nt	GAGATCGTGTGACCCAGTCCCTGCCACCTGTCTGTCTCCGGCGAGAGACCCCTGAG CTGCCGGCCTCCAGTCCGTGCTCTTACCTGGCTGGTATCAGCAGAACCTGGACAGGCC CTAGGCTGTGATCTACGACGCTCCACAGGCTACCGGCATCCCTGCCCGTCTCCGGCTCT GGCTCCGGCACCGACTTCACTGACATCTCCAGCTGGAACCTGAGGACTTCGCGCTGACTA CTGCCAGCAGCGGTCCGACTGGTGTATGATATCTTCCGCGAGGACCAAGCTGGAATCAAGG GCGAGGGGATCTGGCGGAGAGTGGAGGGGGCGGATCCGAAATGAGTGGTGCAGTCT GGCGCGAAGTGAAACCCCTGGCGAGTCCCTGAAGATCTCTGCAAGGCTCCGGCTACACCTT CACCTCTTACTGGATCGGTGGTGGCGAGATCCCTGGCAAGGCGCTGAGTGGATGGGCATCA TCTACCTGGGACTCCGACACCCGCTACTTCCAGCTTCCAGGGCCAGGTGACCTTCTCCGCC GACAAAGTCCATCTCCACCGCTACCTGAGTGGAACTCCCTGAAACCTCCGACACCGCCATGTA CTATTGCGCCACCGCCACCTAGCTACTGCTACTTCCAGCTGTGGCGAGAGCACCCCTGGTGA CCGTGCTTCC
595.	PSMA-L LH x I2C HL	artificial	aa	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRAIGIPARFSGS GSGTDFTLTISSLEPEDFAVYQCQRSDWLMYTFGQGTKLEIKGGGGSGGGGGSEVQLIVQS GAEVKTPGESLKISCKSGSYTFTSYWIGWVRQMPGKGPPEWMGI IYPGDS DTRYSPSFQGVTFSA DKSISTAYLQWNSLKTSDTAMYCATANPSYWFDLWGRGTLIVTSSGGGGSEVQLVSGGGGLVQ PGSLKLSCAASGFTFNKYAMNWRQAPGKLEWVARIRSKYNNYATYYADSVKDRFTISRDDSK NTAYLQMNLIKTEDTAVYYCVRHGNFNSYISWAYWGQGLTIVTSSGGGGSGGGSGGSGQTV VTQEP SLTVSPGGITVLTTCGSSTGAVTSGNYPNWVQKPGQAPRLIGTKFLAPGPARFSGSL LGKKAALTLGTVQPEDEAEYICVLWYNRWVFGGTGKLTIVL
596.	PSMA-L LH x I2C HL	artificial	nt	GAGATCGTGTGACCCAGTCCCTGCCACCTGTCTGTCTCCGGCGAGAGACCCCTGAG CTGCCGGCCTCCAGTCCGTGCTCTTACCTGGCTGGTATCAGCAGAACCTGGACAGGCC CTAGGCTGTGATCTACGACGCTCCACAGGCTACCGGCATCCCTGCCCGTCTCCGGCTCT GGCTCCGGCACCGACTTCACTGACCATCTCCAGCTGGAACCTGAGGACTTCGCGCTGACTA

				CTGCCAGCAGCGGTCCGACTGGCTGATGTATACCTTCGGCCAGGGCACCAGCTGGAATCAAGG GGGAGGGGATCTGGCGGGAGGAGTGGAGGGGGCGGATCCGAAGTGCAGCTGGTGAGTCT GGCGCGAAGTGAAACCCCTGGGAGTCCCTGAAGATCTCTCAAGGGCTCCGGCTACACCTT CACCTCTTACTGGATCGGCTGGTGGCCAGATCCCTGGCAAGGCCCTGAGTGGATGGCATCA TCTACCTTGGGACTCCGACACCCGGTACTCTCCAGCTTCAGGGCCAGGTGACCTTCTCCGCC GACAAAGTCCATCTCACCGCTACCTGCTAGTGAATCCCTGAAACCTCCGACACCGCATGTA CTATTGCCACCGCCACCCCTAGTACTGCTGATCCGAGTGGTGGTGGGAGGAGTGGTGCAG CCGTGCTTCCGAGGTGATGAACTCTCATGTGACCTCTGATTCACCTTCAATAAGTACGCATGAA CTGGTCCGCCAGGCTCCAGGAAAGGTTTGAATGGTTCGCATAGAAGTAAATAATA ATTATGCAACATATATATGCCGATTCAGTGAAGACAGGTTACCATCTCCAGAGATGATCAAAA AACACTGCCATCTACAAATGAACAATGAAACTGAAACTGAGGACACTGCCGTGACTACTGTGAG ACATGGGAACCTTCGGTAAATAGCTACATATCCCTACTGGCTTACTGGGCCAAGGACTTGGTCA CCGTCTCCTCAGGTGGTGGTTCCTGGCGCGCGCTCCGGTGGTGGTCTCACACTGTT GTACTCAGGAACCTTCACTCACCGTATCACTGGTGGTGAACAGTCACTCACTTGTGGTCTC GACTGGGTGTTACATCTGGCAACTACCAAACTGGGTCCAAACAAACAGGTCAAGCACCCC GTGGTCTAAATAGTGGGACTAAGTTCCTCGCCCCGGTACTCTGCCAGATTCTCAGGTCCCTG CTTGAGGCAAGGTGCCCTCACCTCTCAGGGGTACAGCCAGAGATGAGGCAGATATATTACTG TCTTCTATGTTACAGCAACCCCTCGGTCTCCCTGAGGAAACCAACTGACTCTCCTA DIQMTQSPSTLAASAGEKVTITCRASSSVTHHWYQKPKAPKLLIYDTSKVASGVPSRFSGG SGTAFTLTISVVQTDFAFYCQWRSRNSPYTFQGQTKLEIK
597.	PM 99-A8 VL	artificial	aa	GACATCCAGATGACTCAGTCTCCATCAACCTGGCTGCATCTCGGGGGAGAAAGTCACATCAC CTGCCGTGCCAGTCCAGTGTGACTTACATGCACTGGTACCAGCAGAGCCAGCAAGCCCTTA AATTATTGATTATGACACATCCAAAGTGGCTTCTGGAGTCCCAAGTCGCTCAGTGGCAGTGGG TCTGGACCCGATTACTCTCAATCAGTCCCTGCTGAGACTGATGACTTTGCCACTATTACTG TCAGCAGTGGAGTAGGAACTCACCTACACGTTTGGACAGGGACCAAGCTGGAATCAAA RASSSVTYMH DTSKVAS QWRSRNSPYT EVQLLESGGGLVQPGGSLRLSCAASGFTSFDFMAWVRQAPGKLEWVATIVSDGGSTYYRDSVK GRFTISRDNAKNTLYLQMSDLRAEDTAVYCAKRGNSGYVMDAWGQGTIVTSS GAGGTGCAGCTGCTCGAGTCTGGTGGAGGCTTAGTGCAGCTGGAGGTCCCTAAGACTCTCCTG TGACGCTCAGGATTCACTTTCAGTGACTTTTCATGGCTGGTCCGCCAGGCTCCAGGAAGG GGCTGGAGTGGTCCGAACCATTTGTTCTGATGGTGGTAGCACTACTATCGCGACTCCGTGAAG GGCGGTTTCACTATCTCCAGAGATAATGCAAAAACACCTGTACCTGCAATGGACAGTCTGAG GGCTGAGGACACGGCCGTTTATTACTGTGCAAAACCGGCAATTCGGGGTACTATGTTATGGATG CCTGGGTCAAGGAACACTACGGTCAACCGTCTCCTCA
599.	PM 99-A8 LCDR1	artificial	aa	
600.	PM 99-A8 LCDR2	artificial	aa	
601.	PM 99-A8 LCDR3	artificial	aa	
602.	PM 99-A8 VH	artificial	aa	
603.	PM 99-A8 VH	artificial	nt	

604.	PM 99-A8 HCDR1	artificial	aa	DEFMA	TIVSDGGSTYYRDSVKG
605.	PM 99-A8 HCDR2	artificial	aa		RNSGYVMDA
606.	PM 99-A8 HCDR3	artificial	aa		EVQLLESGGGLVQPGGSLRLS
607.	PM 99-A8 HL	artificial	aa		CAASGFTFSDFFMAWVRQAPGKGLEWVATIVSDGGSTYYRDSVK
608.	PM 99-A8 HL	artificial	nt		GRFTISRDNAKNTLYLQMSLSRAEDTAVYCAKRGNSGYVMDAWGQGTIVTVSSGGSGGGGSGS
609.	PM 99-A8 HL x I2C	artificial	aa		GGGSDIQMTQSPSTLAASAGEKVTITCRASSVTYMHVYQKPGKAPKLLIYDTSKVA
610.	PM 99-A8 HL x I2C	artificial	nt		SGVPSR
					FSGSGSGTAFTLTISVQTD
					DFATYYCQWSRNSPYTFGGTKLEIK
					GAGGTGCAGCTGCTCGAGTCTGGTGGAGGCTAGTCAGCCTGGAGGTCCTTAAGACTCTCCTG
					TGCAGCCTCAGGATTACATTTTCAGTGACTTTTTCATGGCTGGTCCGCCAGGCTCCAGGAAGG
					GGCTGGAGTGGTTCGCAACCATTTCTGATGGTGGTAGCACTTACTATCGCGACTCCGTGAAG
					GGCCGTTTCACTATCTCCAGAGATAATGCAAAAACACCTGTACCTGCAATGGACAGTCTGAG
					GGCTGAGGACACGGCCGTTTATTACTGTGCAAAAACGGGCAATTCGGGGTACTATGTATGGATG
					CCTGGGGTCAAGGAACACTACGGTCAACCTCTCCTCAGGTGGTGGTCTGCGGGGGGGCTCC
					GGTGGTGGTGGTCTTGACATCCAGATGACTCAGTCTCCATCAACCTGGCTGCATCTGCGGGGA
					GAAAGTCACCATCACCTGCCGTGCCAGTCCAGTGTGACTTACATGCAGCTGTACCAAGCAAGC
					CAGGCAAGCCCCATAATTAATTGATTATGACACATCCAAAGTGGCTTCTGGAGTCCCAAGTCGC
					TTCAGTGGCAGTGGGTCTGGGACCGCATTTACTCTCACAATCAGCTCCGTCCGTCAGACTGATGACTT
					TGCCACTTATTACTGTTCAGCAGTGGAGTAGAACTCACCTACACGTTTGGACAGGGACCAAGC
					TGAAATCAAA
					EVQLLESGGGLVQPGGSLRLS
					CAASGFTFSDFFMAWVRQAPGKGLEWVATIVSDGGSTYYRDSVK
					GRFTISRDNAKNTLYLQMSLSRAEDTAVYCAKRGNSGYVMDAWGQGTIVTVSSGGSGGGGSGS
					GGGSDIQMTQSPSTLAASAGEKVTITCRASSVTYMHVYQKPGKAPKLLIYDTSKVA
					SGVPSR
					FSGSGSGTAFTLTISVQTD
					DFATYYCQWSRNSPYTFGGTKLEIK
					SGGSEVQLVESGGGLV
					QPGGSLKLSCAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYADSVKDRFTISRDDS
					KNTAYLQMNNLKTEDTAVYCVRHGNGNSYISYWAYWGQGTIVTVSSGGSGGGSGGGGSGT
					VVTQEPSLTVSPGGTIVTLCGSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTPARFSGS
					LLGKKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGTKLTVL
					GAGGTGCAGCTGCTCGAGTCTGGTGGAGGCTTAGTGCAGCCTGGAGGTCCTTAAGACTCTCCTG
					TGCAGCCTCAGGATTACATTTTCAGTGACTTTTTCATGGCTGGTCCGCCAGGCTCCAGGAAGG
					GGCTGGAGTGGTTCGCAACCATTTCTGATGGTGGTAGCACTTACTATCGCGACTCCGTGAAG
					GGCCGTTTCACTATCTCCAGAGATAATGCAAAAACACCTGTACCTGCAATGGACAGTCTGAG
					GGCTGAGGACACGGCCGTTTATTACTGTGCAAAAACGGGCAATTCGGGGTACTATGTATGGATG
					CCTGGGGTCAAGGAACACTACGGTCAACCTCTCCTCAGGTGGTGGTCTGCGGGGGGGCTCC
					GGTGGTGGTGGTCTTGACATCCAGATGACTCAGTCTCCATCAACCTGGCTGCATCTGCGGGGA
					GAAAGTCACCATCACCTGCCGTGCCAGTCCAGTGTGACTTACATGCAGCTGTACCAAGCAAGC
					CAGGCAAGCCCCATAATTAATTGATTATGACACATCCAAAGTGGCTTCTGGAGTCCCAAGTCGC
					TTCAGTGGCAGTGGGTCTGGGACCGCATTTACTCTCACAATCAGCTCCGTCCGTCAGACTGATGACTT

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622.	PM 86-A10 HL	artificial	nt	
623.	PM 86-A10 HL x I2C HL	artificial	aa	
624.	PM 86-A10 HL x I2C HL	artificial	nt	

GGGSDIQMTQSPSTLSASVDRVTITCRASSSVYMHVYQKPKAPKLLIYDTSKVASGVPSR
 FSGSGSGTEFTLTISPPQDDFATYYCQWSRNSPYTFGQTKLEIK
 GAGTGCAGCTGCTCGAGTCTGATGGAGGCTTAGTCAGCCTGGAGGCTCCCTAAACTCTCTG
 TGCAGCCTCAGGATTCACCTTCAGTGACTTTTTCATGGCTGGTCCGCCAGGCTCCAGGGAAGG
 GGCTGGAGTGGTCCGAACCATTTGTTCTGATGGTGGTAGCACTTACTATCGCACTCCGTGAAG
 GGCCGTTTCACTATCTCCAGAGATAATTCAAATAAACCCCTGTACCTGCAATGAACAACTCTGAG
 GTCGAGGACACGGCCGTTTATTACTGTGCAAAACCGGCAATTCCGGGTACTATGTATGGATG
 CCTGGGTCAAGGAACACGGTCAACCTGCTCCCTCAGGTGGTGGTCTTGGCGGGCGGCTCC
 GGTGGTGGTGGTCTGACATCCAGATGACTCAGTCTCCATCAACCTGTCTGCTGCTGTGGGGA
 CAGAGTCACCATCACCTGCCGGCCAGCTCCAGTGTGACTTACATGCACTGTACCAAGCAAGC
 CAGGCAAGCCCTAAATTTATTGATTTATGACACATCCAAAGTGGCTTCTGGAGTCCCAAGTCCG
 TTCAGTGGCAGTGGTCTGGGACCGAATTTACTCTCACAATCAGCTCCCGCAGCTGATGACTT
 TGCCACTTATTACTGTACAGCTGGAGTAGAACTACCCCTACACGTTTGGGCAGGGGACCAAGC
 TGGAAATCAA
 EVQLLESDGGLVQPGSLKLSCAASGFTFSDFMAWVRQAPGKGLEWVATIVSDGGTYRDSVK
 GRFTISRDNKNTLYLQMNLRSEDTAVYYCAKRGNSGYVMDAWGQGTIVTVSSGGSGSGGGS
 GGGSDIQMTQSPSTLSASVDRVTITCRASSSVYMHVYQKPKAPKLLIYDTSKVASGVPSR
 FSGSGSGTEFTLTISPPQDDFATYYCQWSRNSPYTFGQTKLEIKSGGGSEVQLVESGGIV
 QPGSLKLSCAASGFTFNKYAMNWRQAPGKGLEWVARIRSKYNNYATYADSVKDRFTISRDDS
 KNTAYLQMNLRKTEDTAVYYCVRHNGFNSYISYAWWGQGLTVTVSSGGSGSGGSGGGSQT
 VVTQEPSLTVSPGGTTLTLCGSSTGAVTSGNYPNWQKPGQAPRGLIGTKFLAPGTPARFSGS
 LLGKKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGTKITVI
 GAGTGCAGCTGCTCGAGTCTGATGGAGGCTTAGTCAGCCTGGAGGTCCTCTAAACTCTCTG
 TGCAGCCTCAGGATTCACCTTCAGTGACTTTTTCATGGCTGGTCCGCCAGGCTCCAGGGAAGG
 GGCTGGAGTGGTCCGAACCATTTGTTCTGATGGTGGTAGCACTTACTATCGCACTCCGTGAAG
 GGCCGTTTCACTATCTCCAGAGATAATTCAAATAAACCCCTGTACCTGCAATGAACAACTCTGAG
 GTCTGAGGACACGGCCGTTTATTACTGTGCAAAACCGGCAATTCCGGGTACTATGTATGGATG
 CCTGGGTCAAGGAACACGGTCAACCTGCTCCCTCAGGTGGTGGTCTTGGCGGGCGGCTCC
 GGTGGTGGTGGTCTGACATCCAGATGACTCAGTCTCCATCAACCTGTCTGCTGCTGTGGGGA
 CAGAGTCACCATCACCTGCCGGCCAGCTCCAGTGTGACTTACATGCACTGTACCAAGCAAGC
 CAGGCAAGCCCTAAATTTATTGATTTATGACACATCCAAAGTGGCTTCTGGAGTCCCAAGTCCG
 TTCAGTGGCAGTGGTCTGGGACCGAATTTACTCTCACAATCAGCTCCCGCAGCTGATGACTT
 TGCCACTTATTACTGTACAGTGGAGTAGAACTACCCCTACACGTTTGGGCAGGGGACCAAGC
 TGGAAATCAAATCCGAGGTGGTGGATCCGAGTGCAGCTGGTGGTCTGGAGGAGGATGGTG
 CAGCTGGAGGTCATTGAACTCTCATGTGACGCTCTGGATTCACCTTCAATAAGTACGCCAT
 GAACTGGGTCGCCAGGCTCCAGGAAGGTTTGGATGGTGGTCTCGCATAGAGTAATAATA
 ATAATTATGCAACATATTATGCCGATTTCAGTGAAGACAGGTTTACCCTCTCCAGAGATGATTCA

				AAAACACTGCCTATCTACAAATGAACAACCTTGAAAACTGAGGACACTGCCGTGTACTACTGTGT GAGACATGGGAACCTTCGGTAATAGTACATATCTACTGGGCTTACTGGGCCAAGGACTCTGG TCACCGTCTCTCAGGTGGTGGTCTGCGGGCGGGGCTCGGTGGTGGTCTCAGACT GTTGTACTCAGGAACCTTCACTACCGTATCACTGGTGAACAGTACACACTCAGTGTGGCTC CTCGACTGGGCTGTATCATCTGGCAACTCCAACTGGGTCCAAACAAACACAGGTAGGCAC CCGTGGTCTAATAGGTGGACTAGTCTCCCGCCCGGTACTCTCCAGATTCTCAGGCTCC CTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGTACAGCCAGAGGTAGGAGCAATATTA CTGTGTTCTATGTTACAGCAACCGCTGGGTGGTGGAGGAACCAAACTGACTGTCCCTA DIQMTQSPSTLAASPGDRVTTTCRASSSVTYMHVYQQKPKSPKLLIYDTSKVASGVNRFSGSG SGTFTLTITISLQPDIIATYYCQQWSRNSPYTFGGTKLEIK
625.	PM 86-B4-2 VL	artificial	aa	
626.	PM 86-B4-2 VL	artificial	nt	GACATCCAGATGACTCAGTCTCCATCAACCTGGCTGCATCTCCGGGGACAGAGTACCATCAC CTGCCGTGCCAGCTCCAGTGTGACTTACTGCACTGGTACCAGAGAAGCCAGGCAATCCCCCTA AATTATTGATTATGACACATCCAAAGTGGCTTCTGGAGTCCCAATCGCTTCAGTGGCAGTGGG TCTGGACCGGAATTACTCTCAATCAGTCCCTGCAGCTGATGACATTGCCACTTATTACTG TCAGCAGTGGAGTAGGAACTCACCTACACGTTTGACAGGGGACCAAGCTGGAAATCAAA RASSSVTYMH DTSKVAS QQWSRNSPYT
627.	PM 86-B4-2 LCDR1	artificial	aa	
628.	PM 86-B4-2 LCDR2	artificial	aa	
629.	PM 86-B4-2 LCDR3	artificial	aa	
630.	PM 86-B4-2 VH	artificial	aa	EVQLLES DGLVQPGSLRLSCAASGFTFSDEFMAWVRQAPKGLEWVATIVSDGGSTVYRDSVK GREFTSRDNSKNTLYLQMNSLRAEDTAVYCAKRGNSGYVMDAWGQGTIVTVSS
631.	PM 86-B4-2 VH	artificial	nt	GAGGTGCACTGCTCGAGTCTGATGGAGGCTTAGTGCAGCCTGGAGGCTCCCTAAGACTCTCCTG TGAGCCCTCAGGATTCACTTTCAGTGACTTTTCATGGCTGGTCCGCCAGGCTCCAGGGAAGG GGCTGGAGTGGTGGCAACCATTTCTGATGGTGGTAGCACTTACTATCGCGACTCCGCTGAAG GGCGTTTCACTATCTCCAGAGATAATTCAAAAACACCCCTGTACCTGCAAAATGAACAGTCTGAG GGCTGAGGACACGGCCGTTTATTACTGTGCAAAAACCGGCAATTCGGGGTACTATGTTATGGATG CCTGGGGTCAAGGAACACTACGGTCAACCGTCTCCTCA
632.	PM 86-B4-2 HCDR1	artificial	aa	DEEMA
633.	PM 86-B4-2 HCDR2	artificial	aa	TIVSDGGSTVYRDSVKG
634.	PM 86-B4-2 HCDR3	artificial	aa	RGNSGYVMDA
635.	PM 86-B4-2 HL	artificial	aa	EVQLLES DGLVQPGSLRLSCAASGFTFSDEFMAWVRQAPKGLEWVATIVSDGGSTVYRDSVK GREFTSRDNSKNTLYLQMNSLRAEDTAVYCAKRGNSGYVMDAWGQGTIVTVSSGGSGSGGGS GGGSDIQMTQSPSTLAASPGDRVTTTCRASSSVTYMHVYQQKPKSPKLLIYDTSKVASGVNRF FSGSGSGTEFTLTISLQPDIIATYYCQQWSRNSPYTFGGTKLEIK
636.	PM 86-B4-2 HL	artificial	nt	GAGGTGCACTGCTCGAGTCTGATGGAGGCTTAGTGCAGCCTGGAGGTCCTTAAGACTCTCCTG TGAGCCCTCAGGATTCACTTTCAGTGACTTTTCATGGCTGGTCCGCCAGGCTCCAGGGAAGG GGCTGGAGTGGGTCCGAACCATTTGTTCTGATGGTGGTAGCACTTACTATCGCGACTCCGCTGAAG

				GGCGGTTTCACTATCTCCAGAGATAATTCAAAAAACACCCCTGTACCTGCAAAATGAACAGTCTGAG GGCTGAGGACACGGCCGTTTATTACTGTGCAAAACCGGCAATTCGGGGTACTATGTTATGGATG CCTGGGTCAAGAACTACGGTCACCGTCTCCTCAGGTGGTGGTTCGCGGGCGGCGGCTCC GGTGGTGGTGGTCTTGACATCCAGATGACTCAGTCTCCATCAACCCCTGGCTGCATCTCCGGGGGA CAGATCACCATCACCTGCCGTGCCAGTCCAGTGTGACTTACATGCACTGGTACACAGCAAGC CAGGCAATCCCTAAATTATTGATTATGACACATCCAAAGTGGCTCTGGAGTCCCAAATCGC TTCAGTGGCAGTGGTCTGGGACCGAATTACTTCACAATCAGTCCCTGCAGCCTGATGACAT TGCCACTTATTACTGTGACAGTGGAGTAGGAACCTACCCCTACACGTTTGGACAGGGGACCAAGC TGGAATCAAA
637.	PM 86-B4-2 HL x I2C HL	artificial	aa	EVQLLES DGLVQPGSLRLSCAASGFTFSDPFMAWVRQAPGKLEWVATIVSDGGSTYYRDSVK GRFTISRDN SKNTLYIQMNSLRAEDTAVYYCAKRGNSGYVMDAWGQGTIVTVSSGGSGSGGGS GGGSDIQMTQSPSTLAASPGDRVITICRASSVTYMHVYQKPGKSPKLLIYDTSKVASGVPNR FSGSGSGTEFTLTISSLQPDIIATYCCQWSRNSPYTFGQGTQKLEIKSGGGSEVQLVESGGGLV QPGSLKLSCAASGFTFNKYAMNWRQAPGKLEWVATIRSKYNNYATYYADSVKDRFTISRDDS KNTAYLQMNLLKTEDTAVYYCVRHGFGNSYISYWAYWGQGLTVTVSSGGSGGGSGGGSGGTSQT VVTQEPSLTVSPGGTVTLTCGSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTPARFSGS LLGKKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGTKLTVL
638.	PM 86-B4-2 HL x I2C HL	artificial	nt	GAGTGCAGCTGCTCGAGTCTGATGGAGGCTTACTGCAGCCTGGAGGTCCTTAAGACTCTCCTG TGCAGCCTCAGGATTCATTTAGTACTTTTTCATGGCCTGGTCCGCCAGGCTCCAGGGAAGG GGCTGGAGTGGTGGCAACCATTTGTTCTGATGGTGGTAGCACTACTATCCGCACTCCGTGAAG GGCGGTTTCACTATCTCCAGAGATAATTCAAAAACACCCCTGTACCTGCAAAATGAACAGTCTGAG GGCTGAGGACACGGCCGTTTATTACTGTGCAAAACCGGCAATTCGGGTACTATGTTATGGATG CCTGGGTCAAGGAACTACGGTCACCGTCTCCTCAGGTGGTGGTGTCTGGCGGGCGGCTCC GGTGGTGGTGGTCTTGACATCCAGATGACTCAGTCTCCATCAACCCCTGGCTGCATCTCCGGGGGA CAGATCACCATCACCTGCCGTGCCAGTCCAGTGTGACTTACATGCACTGGTACCAAGCAAGC CAGGCAATCCCTAAATTATTGATTATGACACATCCAAAGTGGCTCTGGAGTCCCAAATCGC TTCAGTGGCAGTGGTCTGGGACCGAATTACTCTCACAATCAGTCCCTGCAGCCTGATGACAT TGCCACTTATTACTGTGACAGTGGAGTAGGAACCTACCCCTACACGTTTGGACAGGGGACCAAGC TGGAAATCAAAATCCGAGGTGGTGGATCCGAGGTGCAGTGGTTCGAGTCTGGAGGAGGATTGGTG CAGCCTGGAGGGTCATTGAACTCTCATGTGAGCTCTGGATTCACCTTCAATAAGTACGCCAT GAACTGGTCCGCGAGGCTCCAGGAAAGGTTTGGAAATGGTGTCTGCGATAGAAATAATATA ATAATTATGCAACATATTATGCCGATTGAGTGAAGAACAGAGTTCAACCATCTCCAGAGATGATTCA AAAAACACTGCCATCTACAAATGAACAATGAACAATGAGGACACTGCCGTGACTACTGTGTGT GAGACATGGGAACTTCGGTAATAGTACATATCTTACTGGCTTACTGGGGCAAGGACTCTGG TCACCGTCTCCTCAGGTGGTGGTCTTGGCGCGCGGCTCCGGTGGTGGTGGTCTCTCAGACT GTTGTGACTCAGGAACCTTCACTCACCGTATCACTGGTGAACAGTCACTCACTTGTGGCTC CTCGACTGGGGCTGTACATCTGGCAACTACCAAACTGGGTCCAAACAAACAGGTCAGGCAC

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				<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>
<p>651.</p> <p>PM 98-B4 HL x 12C HL</p>	<p>artificial</p> <p>aa</p>			<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>
<p>652.</p> <p>PM 98-B4 HL x 12C HL</p>	<p>artificial</p> <p>nt</p>			<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>
<p>653.</p> <p>PM 86-C3 VL</p>	<p>artificial</p> <p>aa</p>			<p>5</p> <p>10</p> <p>15</p> <p>20</p> <p>25</p> <p>30</p>

654.	PM 86-C3 VL	artificial	nt	GACATCCAGATGACTCAGTCTCCATCAACCCCTGGTGTGATCTGTGGGGACAGAGTACCATCAC CTGCCGTGCCAGCTCCAGTGTGACTTACATGCTGTGATCCAGCAGAGCCAGGCAAGCCCTTA AATTATTGATTATGACACATCCAAAGTGGCTTCTGGAGTCCAAATCGCTTCAGTGGCAGTGGG TCTGGACCGAATTTACTCTCACAATCAGCTCCCTGCAGACTGATGACTCTGCCACTTATTACTG TCAGAGTGGAGTAGGAACTCACCCCTACACGTTTGGACAGGGGACCAAGCTGGAATCAAA
655.	PM 86-C3 LCDR1	artificial	aa	RASSVTYMH
656.	PM 86-C3 LCDR2	artificial	aa	DTSKVAS
657.	PM 86-C3 LCDR3	artificial	aa	QQWSRNSPYT
658.	PM 86-C3 VH	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAASGFTFDFFWAVRQAPGKLEWVATIVSDGGSTYYRDSVK GRFTISRDNAKNTLYLQMNSLTAEDTAIYCAKRGNSGYVMDANGQGTIVTVSS
659.	PM 86-C3 VH	artificial	nt	CAGGTGCAGCTGCTCGAGTCTGGTGGAGGCTTAGTGCAGCCTGGAGGTCCTAAACCTCCTG TGCAGCCTCAGGATTCACCTTCAGTGACTTTTCAATGGCTGGTCCGCCAGGCTCCAGGAAGG GGCTGGAGTGGTCCCAACCATTTCTGATGGTGGTAGCACTTACTATCGTGACTCCGTGAAG GGCCGTTTCACTATCTCCAGAGATAATGCAAAAAACACCTGTACCTGCAATGAACAGTCTGAC GGCTGAGGACACGGCCATTTATTACTGTGCAAAACGCGCAATTCGGGGTACTATGTATGGATG CCTGGGTCAAGGAACTACGGTCAACCGTCTCCTCA
660.	PM 86-C3 HCDR1	artificial	aa	DFFWA
661.	PM 86-C3 HCDR2	artificial	aa	TIVSDGGSTYYRDSVKG
662.	PM 86-C3 HCDR3	artificial	aa	RGNSGYVMDA
663.	PM 86-C3 HL	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAASGFTFDFFWAVRQAPGKLEWVATIVSDGGSTYYRDSVK GRFTISRDNAKNTLYLQMNSLTAEDTAIYCAKRGNSGYVMDANGQGTIVTVSSGGSGGGGS GGGSDIQMTQSPSTLAASVGRVTITCRASSSVTVMHWYQKPKAPKLLIYDTSKVASGVPNR FSGSGSTEFTLTISLQTDSDSATYQCQWSRNSPYTFGQGTKLEIK
664.	PM 86-C3 HL	artificial	nt	GAGGTGCAGCTGCTCGAGTCTGGTGGAGGCTTAGTGCAGCCTGGAGGTCCTAAACCTCCTG TGCAGCCTCAGGATTCACCTTCAGTGACTTTTCAATGGCTGGTCCGCCAGGCTCCAGGAAGG GGCTGGAGTGGTCCCAACCATTTCTGATGGTGGTAGCACTTACTATCGTGACTCCGTGAAG GGCCGTTTCACTATCTCCAGAGATAATGCAAAAAACACCTGTACCTGCAATGAACAGTCTGAC GGCTGAGGACACGGCCATTTATTACTGTGCAAAACGCGCAATTCGGGGTACTATGTATGGATG CCTGGGTCAAGGAACTACGGTCAACCGTCTCCTCAGGTGGTGGTCTGGCGGGGGGGCTCC GGTGGTGGTGGTCTGACATCCAGATGACTCAGTCTCCATCAACCTGGTGCATCTGGGGGA CAGAGTCAACCATCACCTGCCGTGCCAGTCCAGTGTGACTTACATGCACCTGGTACACAGAGAAGC CAGGCAAGCCCCATAATTATTGATTATGACACATCCAAAGTGGCTTCTGGAGTCCCAATCGC TTCAGTGGCAGTGGGTCTGGGACCGAATTTACTCTCACAATCAGTCCCTGCAGACTGATGACTC TGCCACTTATTACTGTGACAGTGGAGTAGGAACTCACCTACACGTTTGGACAGGGGACCAAGC TGAATAATCAAA
665.	PM 86-C3 HL x 12C	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAASGFTFDFFWAVRQAPGKLEWVATIVSDGGSTYYRDSVK

	HL				GRFTISRDNAKNTLYLQMNSLTAEDTAIYCAKRGNSGYVMDAWGQGTTVTVSSGGSGSGSGS GGGSDIQMTQSPSTLAASVGDRTITCRASSSVTYMHWYQKPKAPKLLIYDTSKVASGVPNR FSGSGSGTEFTLTISSLQDDSATYCYQQWSRNSPYTFQGQTKLEIKSGGGSEVQLVESGGGLV QPGSLKLSCAASGFTFNKYAMNVRQAPGKLEWARIIRSKYNNYATYADSVKDRFTISRDDS KNTAYLQMNLLKTEDTAVYYCVRHGNEFSYISYWAYWGQGLTVTVSSGGSGSGSGSGSGSQT VVTQEPSLTVSPGGTVTLTCSSTGAVTSGNYPNVWQKPGQAPRGLIGGTRKFLAPGPARFSGS ILGGKAALTLSGVQPEDEAEYYCVLWYSNRWFGGTKLTVL
666.	PM 86-C3 HL x 12C HL	artificial	nt		GAGGTGCAGCTGCTCGAGTCTGGTGGAGGCTTAGTGCAGCTGGAGGGTCCCTAAACTCTCCTG TGCAGCCTCAGGATTACATTTTCAGTGACTTTTTCATGGCTGGTCCGCCAGGCTCCAGGAAGG GGCTGGAGTGGTGCACCAACATTGTTCTGATGGTGGTAGCACTTACTATCGTACTCCGTGAAG GGCGTTTCACTATCTCCAGAGATAATGCAAAAACACCTGTACCTGCAATGAACAGACTGAC GGCTGAGGACACGGCCATTTATTACTGTGCAAAACCGGGAATTCGGGTACTATGTATGGATG CCTGGGTCAAGGAACACTACGTCACCGTCTCTCAGGTGGTGGTTCCTGGCGGCGGCGCTCC GGTGGTGGTGGTTCGACATCCAGATGACTCAGTCTCCATCAACCTGGCTGCATCTGTGGGGA CAGAGTCACCATCACCTGCCGTGCCAGTCCAGTGTACTTACATGCATGCTGTACAGCAGAGAAGC CAGGCAAGCCCCATAATTATTGATTATGACACATCCAAAGTGGCTTCTGGAGTCCAAATGCG TTCAGTGGCAGTGGTCTGGGACCGAATTAATCTCAATCACTCCCTGCAGACTGATGACTC TGCCACTTATTACTGCAGCAGTGGAGTAGGAACACCTACACGTTTGGACAGGGAACCAAGC TGGAAATCAATCCGGAGGTGGTGGATCCAGGTGCAGTGGTGCAGTCTGGAGGAGGATGGTG CAGCTGGAGGTCAATTGAACTCTCATGTGCAGCTCTGGATTCACCTTCAATAGTACGCCAT GAACTGGTCCGCCAGGCTCCAGGAAGGTTTGGATGGTTCCTGCGCATAGAAAGTAATATA ATAATTATGCAACATATTATGCCGATTCTAGTGAAGACAGGTTTACCCTCTCCAGAGATGATCA AAAAACACTGCCTATCTACAAATGAACAACCTGAAAACTGAGGACACTGCCGTGACTACTGTGT GAGACATGGGAACCTTCGGTAATAGCTACATACTACTGGGCTTACTGGGCCAAGGACTCTGG TCACCGTCTCTCAGGTGGTGGTGGTCTGGCGGCGGCGCTCCGGTGGTGGTGGTCTCAGACT GTTGTGACTCAGGAACCTTCACTACCGTATCACTGGTGGAAACAGTCACTCACTTGTGGCTC CTGACTGGGCTGTACATCTGGCACTACCCAACTGGTCCAAACAAACCAGGTAGGCAC CCCGTGGTCTAATAGTGGGACTAAGTCTCCGCCCCCGGTACTCCTGCCAGATTCTCAGGCTCC CTGCTTGGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCAGAGGATGAGGCAAGATTA CTGTGTTCTATGGTACAGCAACCGCTGGGTGGTGGAGGAACCAACTGACTGTCTCTA
667.	PM 86-E12 VL	artificial	aa		DIQMTQSPSTLSAGDRVTITCRASSSVTYMHWYQKPGTAPKLLIYDTSKVASGVSRFSGSG SGTEFTLTISVVQPEDIAIYYCQQWSRNSPYTFQGQTKLEIK
668.	PM 86-E12 VL	artificial	nt		GACATCCAGATGACTCAGTCTCCATCAACCTGTCTGCACTCGGGGGGACAGAGTCAACATCAC CTGCCGTGCCAGCTCCAGTGTGACTTACATGCACTGGTACAGAGAAGCCAGGCACAGCCCTTA AATTATTGATTATGACACATCCAAAGTGGCTTCTGGAGTCCCAAGTCGCTCAGTGGCAGTGG TCTGGGACCGGAATTACTCTCAATCACTCCGTCCGTGAGCCTGAAGACATTGCCACTTACTG TCAGCAGTGGAGTAGGAACTCACCTTACAGTGTGGACAGGACCAAGCTGGAATCAAA

669.	PM 86-E12 LCDR1	artificial	aa	RASSVTYMH	5
670.	PM 86-E12 LCDR2	artificial	aa	DTSKVAS	10
671.	PM 86-E12 LCDR3	artificial	aa	QQWSRNSPYT	15
672.	PM 86-E12 VH	artificial	aa	EVQLLESGGGLVQPGGSLRLS	20
673.	PM 86-E12 VH	artificial	nt	CAASGFTFSDFFMAWVRQAPT	25
674.	PM 86-E12 HCDR1	artificial	aa	KGLEWVSTIVSDGGSTYYRDSVK	30
675.	PM 86-E12 HCDR2	artificial	aa	GRFTISRDNKNTLYLQMN	35
676.	PM 86-E12 HCDR3	artificial	aa	SLRAEDTAVYICARRNSGYVMD	40
677.	PM 86-E12 HL	artificial	aa	AWGQGTIVVSS	45
678.	PM 86-E12 HL	artificial	nt	GAGTTCAGCTCGAGTCTGGT	50
679.	PM 86-E12 HL x 12C HL	artificial	aa	GAGTTCAGCTCGAGTCTGGT	55

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687.	PM F1-A10 VH	artificial	nt	GAGTGCAGCTGCTCGAGTCTGGTGGAGGCTTAGTGCAGCCTGGAGGGTCCCTAAGACTCTCCTG TGCAGCCTCAGGATTCACTTTCAGTGACTTTTTCATGGCTGGTCCGCCAGGCTCCAGGAGGG GGCTGGAGTGGTCTCAACCATTTTCTGATGGTGGTAGCACTTACTATCGGACTCCGTGAAG GGCGTTTCACTATCTCCAGAGATAATTCAAAAAACACCTGTACCTGCAATGAACACTCTGAG GGCTGAGGACACGGCGTTTATTACTGTGCAAGACGGGCAATTCGGGGTACTATGTATGGATG CCTGGGTCAAGGAACACTACGGTCAACCGTCTCCTCA
688.	PM F1-A10 HCDR1	artificial	aa	DFEWA
689.	PM F1-A10 HCDR2	artificial	aa	TIVSDGGSTYYRDSVKG
690.	PM F1-A10 HCDR3	artificial	aa	RNSGYVYVMDA
691.	PM F1-A10 HL	artificial	aa	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFFMAWVRQAPGRGLEWVSTIVSDGGSTYYRDSVK GRFTISRDN SKNTLY LQMNSLRAEDTAVYICARRNGSYVYVMDAWGQGTIVTVSSGGSGGGGS GGGSDIQMTQSPSTLSASVGDRTITCRASSSYVMHWYQQKPKAPKLLIYDTSKVASGVPSR FSGSGSGTEFTLTISSLQPDFAFYCQQWSRNSPYTFGGTKLEIK
692.	PM F1-A10 HL	artificial	nt	GAGTGCAGCTGCTCGAGTCTGGTGGAGGCTTAGTGCAGCCTGGAGGGTCCCTAAGACTCTCCTG TGCAGCCTCAGGATTCACTTTCAGTGACTTTTTCATGGCTGGTCCGCCAGGCTCCAGGAGGG GGCTGGAGTGGTCTCAACCATTTTCTGATGGTGGTAGCACTTACTATCGGACTCCGTGAAG GGCGTTTCACTATCTCCAGAGATAATTCAAAAAACACCTGTACCTGCAATGAACACTCTGAG GGCTGAGGACACGGCGTTTATTACTGTGCAAGACGGGCAATTCGGGGTACTATGTATGGATG CCTGGGTCAAGGAACACTACGGTCAACCGTCTCCTCAGGTGGTGGTCTCGCGGCGCGCTCC GGTGGTGGTGGTCTGACATCCAGATGACTCAGTCTCCATCAACCTGTCTGCTGTGGGGGA CAGAGTCACCATCACCTGCCGGGCCAGCTCCAGTGTGACTTACATGCACCTGGTACAGAGAAGC CAGGCAAGCCCCATAATTATTGATTATGACACATCCAAAGTGGCTTCTGGAGTCCCAAGTCGC TTCAGTGGCAGTGGTCTGGGACCGAATTACTCTCACAATCAGTCCCTGCAGCCTGATGACTT TGCCACTTATTACTGTGAGCAGTGGAGTAGGAACCTACCCCTACACGTTTGGGCAGGGACCAAGC TGGAATCAAA
693.	PM F1-A10 HL x I2C HL	artificial	aa	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFFMAWVRQAPGRGLEWVSTIVSDGGSTYYRDSVK GRFTISRDN SKNTLY LQMNSLRAEDTAVYICARRNGSYVYVMDAWGQGTIVTVSSGGSGGGGS GGGSDIQMTQSPSTLSASVGDRTITCRASSSYVMHWYQQKPKAPKLLIYDTSKVASGVPSR FSGSGSGTEFTLTISSLQPDFAFYCQQWSRNSPYTFGGTKLEIKSGGGSEVQLVESGGGLV QPGGSLKLSCAASGFTFNKYAMNVRQAPGKLEWVARIRSKYNNYATYYADSVKDRFTISRDDS KNYAYLQMNNLKTEDTAVYICVRHGFNGSYISYWAYWGQGLTVTVSSGGSGGGSGGGSSQT VVTQEPSLTVSPGGTVTLICGSSTGAVTSGNYPNWVQKPKQAPRGLIGGTFKFLAPSTAFPSGS LLGGKAALTLSGVQPEDEAEYCYVLWYSNRWVTFGGTKLTVL
694.	PM F1-A10 HL x I2C HL	artificial	nt	GAGTGCAGCTGCTCGAGTCTGGTGGAGGCTTAGTGCAGCCTGGAGGGTCCCTAAGACTCTCCTG TGCAGCCTCAGGATTCACTTTCAGTGACTTTTTCATGGCTGGTCCGCCAGGCTCCAGGAGGG GGCTGGAGTGGTCTCAACCATTTTCTGATGGTGGTAGCACTTACTATCGGACTCCGTGAAG GGCGTTTCACTATCTCCAGAGATAATTCAAAAAACACCTGTACCTGCAATGAACACTCTGAG GGCGTTTCACTATCTCCAGAGATAATTCAAAAAACACCTGTACCTGCAATGAACACTCTGAG

				GGCTGAGGACACGGCCGTTTATTACTGTGCAAGACGGGCAATTCCGGGGTACTATGTTATGGATG CCTGGGGTCAAGGAACCTACGGTCACCGTCAACCTCTCCTCAGGTGGTGGTGGTCTTGGCGGGCGGCTCC GGTGGTGGTGGTCTGACATCCAGATGACTCAGTCTCCATCAACCTGTCTGCATCTGTGGGGA CAGAGTCACCATCACCTGCCGGCCAGTCCAGTGTGACTTACATGCACCTGTTACCCAGACAAGC CAGCAAAAGCCCCATAAATTATGATTTATGACACATCAAAAGTGGCTTCTGGAGTCCCAAGTCGC TTCAGTGGCAGTGGTCTGGACCCGAATTACTCTCAAAATCAGTCCCTGCAGCCTGATGACTT TGCCACTATTACTGTACAGCAGTGGAGTAGAACTCACCTACACGTTTGGCAGGGACCAAGC TGGAAATCAAAATCCGGAGGTGGTGGATCCAGGTGCAGTGGTGCAGTCTGGAGGTGGAGGAGGATTGGTG CAGCCTGAGGGTCATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAATAAGTACGCCAT GAACTGGTCCGCCAGGCTCCAGGAAGGGTTTGAATGGTGTCTCGCATGAAGAATAATATA ATAATTATGCAACATATTATGCCGATTCACTGAAGACAGGTTCAACCATCTCCAGAGATGATTCA AAAAACATGCCTATCTACAAATGAACAACTTGAAAACTGAGGACACTGCCGTGTACTACTGTGT GAGACATGGGAACCTTCGGTAATAGTACATACTCACTGGGCTTACTGGGCCAAGGGACTCTGG TCACCGTCTCCTCAGTGGTGGTGGTCTGCGGGCGGGCTCCGGTGGTGGTCTCTCAGACT GTTGTGACTCAGGAACCTTCACTCACCGTATCACCTGGTGGAACTGACACTCACTTGTGGCTC CTCGACTGGGCTGTTACATCTGCCAACTACCCAAACTGGGTCCAAACAAAACCCAGGTCAAGCAC CCCGTGGTCTAATAGTGGGACTAAGTTCCTGCCCGGGTACTCCTGCCAGATTCTCAGGCTCC CTGCTTGAGGCAAGGCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAAATATTA CTGTCTTCTATGGTACAGCAACCCCTGGGTCTTCGGTGCAGCAACCAACTCACTGTCCTA
695.	PM 99-F1 VL	artificial	aa	DIQMTQSPSTLSASVGRVTITCRASSSVTYMHVYQKPKSKPLLIYDFSKVASGVPSRFSGSG SGTSFTLTISLQPEDIAITYCQQWSRNSPYTFGGQTKLEIK
696.	PM 99-F1 VL	artificial	nt	GACATCCAGATGACTCAGTCTCCATCAACCTGTCTGCATCTGTGGGGGACAGAGTCACCATCAC CTGCCGTGCCAGCTCCAGTGTGACTTACATGCACTGGTACCAGCAGAGCCAGGCAATCCCCCTA AATTATTGATTATGACACATCCAAAGTGGCTTCTGGAGTCCCAAGTCCGCTCAGTGGCAGTGGG TCTGGGACCTCATTTACTCTCACAAATCAGTCCCTGCAGCCTGAAGACATATGSCACTTATTACTG TCAGCAGTGGAGTAGGAACTCACCTTACAGTTTGGACAGGGGACCAAGCTGGAATCAAA
697.	PM 99-F1 LCDR1	artificial	aa	RASSSVTYMH
698.	PM 99-F1 LCDR2	artificial	aa	DTSKVAS
699.	PM 99-F1 LCDR3	artificial	aa	QQWSRNSPYT
700.	PM 99-F1 VH	artificial	aa	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFFMAWVRQAPGRGLEWVSTIVSDGGSTYYRDSVK GRFTISRDNKNTLYLQMNSLRAEDTAVYYCARRNGSGYVMDAWGQGTFTVYSS
701.	PM 99-F1 VH	artificial	nt	GAGTGCAGTGTCTCGAGTCTGGTGGAGGCTTAGTCAGCCTCGAGGGTCCCTAAGACTCTCCTG TGCAGCCTCAGGATTCACTTTCAGTACTTTTCTAGTGGCTGGTCCGCCAGGCTCCAGGGAGGG GGCTGGAGTGGGTCTCAACCATTTGTTCTGTGTTGTGAGTGTGAGTACTACTATCGGACTCCGTGAAG GGCGGTTTCACTATCTCCAGAGATAATTCAAATAAACACCCCTGTACCTGCAAAATGAACAGTCTGAG GGCTGAGGACACGGCCGTTTATTACTGTGCAAGACCGGCAATTCCGGGTACTATGTTATGGATG CCTGGGGTCAAGGAACCTACGGTCACCGTCTCCCTCA

702.	PM 99-F1 HCDR1	artificial	aa	DFFMA	TIVSDGGSTYYRDSVKG
703.	PM 99-F1 HCDR2	artificial	aa		RGNSGYVVMDA
704.	PM 99-F1 HCDR3	artificial	aa		EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFFMWVRQAPGRGLEWVSTIVSDGGSTYYRDSVK
705.	PM 99-F1 HL	artificial	aa		GRFTISRDNKNTLYLQMNSLRAEDTAVYICARRNGSYVMDAWGQGTIVTVSSGGSGGGGS
					GGGSDIQMTQSPSTLSASVGRVTITCRASSSVYMHVYQOKPGKSPKLLIYDTSKVASGVPSR
					FSGSGSTFTLTISLQPEDIAITYCQWSRNSPYTFGGTKLEIK
706.	PM 99-F1 HL	artificial	nt		GAGGTGAGCTGCTCGAGTCTGGTGGAGCTTAGTGACGCTGGAGGTCCTAAGACTCTCCTG
					TGCAGCCTCAGGATTCACTTTCAGTGACTTTTCATGGCCTGGTCCGCCAGGCTCCAGGAGGG
					GGCTGGAGTGGTCTCAACCATTTCTGATGGTGTAGCACTTACTATCGCGACTCCGTGAAG
					GGCCGTTTCACTATCTCCAGAGATAATCAAAAAACACCTGTACCTGCAATGAACACTCTGAG
					GGCTGAGGACACGGCCGTTTATTACTGTGCAAGACACGGCAATTCGGGGTACTATGTATGGATG
					CCTGGGTCAAGAACTACGCTACCGTCTCCTCAGGTGGTGGTTCCTGGCGGCGCGCTCC
					GGTGTGGCGGTTCTGACATCCAGATGACTCAGTCTCCATCAACCTGTCTGCTGTGGGGA
					CAGAGTACCATCACCTGCCGTGCCAGTCCAGTGTGACTTACATGCACGTGGTACACAGAAAGC
					CAGGCAATCCCCTAAATTATTGATTATGACATCCAAAGTGGCTTCTGGAGTCCCAAGTCGC
					TTCAGTGGCAGTGGTCTGGGACCTCATTACTCTCAATCAGTCCCTGCAGCCTGAAGACAT
					TGCCACTTATTACTGTACGAGTGGAGTAACTACCCCTACACGTTTGGACAGGGGACCAAGC
					TGGAATCAAA
707.	PM 99-F1 HL x I2C HL	artificial	aa		EVQLLESGGGLVQPGGSLRLSCAASGFTFSDFFMWVRQAPGRGLEWVSTIVSDGGSTYYRDSVK
					GRFTISRDNKNTLYLQMNSLRAEDTAVYICARRNGSYVMDAWGQGTIVTVSSGGSGGGGS
					GGGSDIQMTQSPSTLSASVGRVTITCRASSSVYMHVYQOKPGKSPKLLIYDTSKVASGVPSR
					FSGSGSTFTLTISLQPEDIAITYCQWSRNSPYTFGGTKLEIKSGGGSEVQLVPSGGGLV
					QPGSLKLSCAASGFTFNKYAMNWRQAPGKLEWVARI RSKYNNYATYYADSVKDRFTISRDDS
					KNTAYLQMNHLKTEDTAVYYCVRHGFNGSYISYWAYWGQGLTVTVSSGGSGGGSGGSGQT
					VVTQEPSLTVSPGGTVTLTCGSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTPARFSGS
					LLGKKAALTLSGVQPEDEAEYYCVLWYSNRWFGGTKLIVL
708.	PM 99-F1 HL x I2C HL	artificial	nt		GAGGTGAGCTGCTCGAGTCTGGTGGAGGCTTAGTGACGCTGGAGGTCCTAAGACTCTCCTG
					TGCAGCCTCAGGATTCACTTTCAGTGACTTTTCATGGCCTGGTCCGCCAGGCTCCAGGAGGG
					GGCTGGAGTGGTCTCAACCATTTCTGATGGTGTAGCACTTACTATCGCGACTCCGTGAAG
					GGCCGTTTCACTATCTCCAGAGATAATCAAAAAACACCTGTACCTGCAATGAACACTCTGAG
					GGCTGAGCACACGGCCGTTTATTACTGTGCAAGACACGGCAATTCGGGGTACTATGTATGGATG
					CCTGGGTCAAGAACTACGCTACCGTCTCCTCAGGTGGTGGTTCCTGGCGGCGCGCTCC
					GGTGTGGCGGTTCTGACATCCAGATGACTCAGTCTCCATCAACCTGTCTGCTGTGGGGA
					CAGAGTACCATCACCTGCCGTGCCAGTCCAGTGTGACTTACATGCACGTGGTACACAGCAAGC
					CAGGCAATCCCCTAAATTATTGATTATGACATCCAAAGTGGCTTCTGGAGTCCCAAGTCGC
					TTCAGTGGCAGTGGTCTGGGACCTCATTACTCTCAATCAGTCCCTGCAGCCTGAAGACAT

55					TGCCACTTATTACTGTACAGTGGAGTAGGAATCAACCTACCCCTACACGTTTGGACAGGGACCAAGC TGGAAATCAATCCGAGGTGGTGGATCCAGGTGCGAGTGGTGGATCGAGTCTGGAGGAGGATGGTG CAGCTGGAGGTCATTGAACTCTCATGTGACGCTCTGGATTCACCTTCAATAAGTACGCCAT GAACTGGTCCGCCAGGCTCCAGGAAGGTTTGGAAATGGTTCCTGCATAGAGTAATATA ATAATTATGCAACATATTATGCCGATTCACTGAAAGACAGGTTTCAACATCTCCAGAGATGATTCA AAAAACACTGCCTATCTACAAATGAACAATGAAACTGAGGACACTGCGGTGTAAGTCTGT GAGACATGGGAACCTTCGTAATAGCTACATATCTACTGGGCTTACTGGGCCAAGGACTCTGG TCACCGTCTCTCAGGTGGTGGTCTGGCGGGCGGCTCCGGTGGTGGTCTCAGACT GTTGTACTCAGGAACCTTCACTACCGTATCACTGGTGAACAGTCACTCACTTGTGGCTC CTGACTGGGCTGTACATCTGGCACTACCCAACTGGTCCAAACAAACCCAGGTCAGGCAC CCCGTGGTCTAATAGGTGGACTAAGTCTCGCCCCCGGCTACTCCTGCCAGATTCTCAGGCTCC CTGCTTGAGGCAAGGCTGCCCTCACCTCTCAGGGTACAGCCAGAGGATGAGGCAGAAATATA CTGTGTTCTATGGTACAGCAACCGCTGGGTCTCGGTGGAGGACCAAACTGACTGTCTCTA DIQMTQSPSTLSASVGDRVTITCRASSSVTYMHYQQKPKSPKLLIYDTSKVASGVPSRFSGSG SGTEFTLTITSSLPDDFATYYCQQWSRNSPYTFGGTKLEIK
709.	PM 99-F5 VL	artificial	aa		GACATCCAGATGACTCAGTCTCCATCAACCTGTCTGCATCTGTGGGGACAGAGTCACCATCAC CTGCGGTGCCAGCTCCAGTGTGACTTACATGCACTGGTACCAGAGAGCCAGGCAAAATCCCCCTA AATTATTGATTATGACACATCCAAAGTGGCTTCTGGAGTCCCAAGTCCGCTTCAGTGGCAGTGGG TCTGGACCGGAATTTACTCTCACAATCAGTCCCTGCAGCCTGATGACTTGGCACTTATTACTG TCAGCAGTGGAGTAGGAACTCACCTACACGTTTGGACAGGGACCAAGCTGGAAATCAAA RASSSVTYMH
710.	PM 99-F5 VL	artificial	nt		DTSKVAS
711.	PM 99-F5 LCDR1	artificial	aa		QQWSRNSPYT
712.	PM 99-F5 LCDR2	artificial	aa		EVQLLESGGGLVQPGGSLKLSCAASGFTFSDFFMAWVRQAPGKLEWVSTIVSDGGSTYYRDSVK
713.	PM 99-F5 LCDR3	artificial	aa		GRFTISRDN SKNTLYLQMN SLTAEDTAIYYCAKRGNSGYVMDAWGQGTITVTVSS
714.	PM 99-F5 VH	artificial	aa		GAGTGCAGCTGCTCGAGTCTGGTGGAGGCTTAGTCAGCCTGGAGGTCCTCTAAACTCTCCTG TGCAGCCTCAGGATTCACCTTCAGTACTTTTCATGGCCTGGTCCGCCAGGCTCCAGGGAAGG GGCTGGAGTGGTCTCAACCATTTGTTCTGATGGTGTAGCACTTACTATCGCGACTCCGTGAAG GGCGTTTCACTATCTCCAGAGATAATTCAAAAAACACCCCTGTACCTGCAATGAACAGTCTGAC GGCTGAGGACACGGCCATTTATTACTGTGCAAAACCGGCAATTCGGGGTACTATGTTATGGATG CCTGGGTC AAGGAAC TACGGTCA CCGTCTCCTCA
715.	PM 99-F5 VH	artificial	nt		DDFWA
716.	PM 99-F5 HCDR1	artificial	aa		TIVSDGGSTYYRDSVKG
717.	PM 99-F5 HCDR2	artificial	aa		RGNSGYVMDA
718.	PM 99-F5 HCDR3	artificial	aa		EVQLLESGGGLVQPGGSLKLSCAASGFTFSDFFMAWVRQAPGKLEWVSTIVSDGGSTYYRDSVK
719.	PM 99-F5 HL	artificial	aa		GRFTISRDN SKNTLYLQMN SLTAEDTAIYYCAKRGNSGYVMDAWGQGTITVTVSSGGGGSGGGGS

720.	PM 99-F5 HL	artificial	nt	GGGSDIQMTQSPSTLSASVGDRVITITCRASSSVTYMHVYQKPKSPKLLIYDTSKVASGVPSR FSGSGTEFTLTIISSLPDDFATYYCQWSRNSPYTFGQGTKLEIK GAGTGCAGCTGCTCGAGTCTGGTGGAGGCTTAGTGCAGCCTGGAGGTCCTAAAACTCTCCTG TGCAGCCTCAGGATTCACCTTTCAGTACTTTTTCATGCCCTGGTCCGCCAGGCTCCAGGGAAGG GGCTGAGTGGTCTCAACCATTTCTGATGGTGGTAGACTTACTATCGGACTCCGTAAG GGCGTTTCACTATCTCCAGAGATAATTCAAAAAACACCTGTACCTGCAATGAACAGTCTGAC GGCTGAGCACACGGCCATTTATTACTGTGCAAAACCGGCAATTCGGGTACTATGTTATGATG CCTGGGTCAAGGAACACGGTCAACCTCTCTCAGGTGGTGGTCTGTGATCTGTGGGGTCC GGTGGTGGTGGTCTGACATCCAGATGACTCAGTCCAGTCCAGTCCAGTCCAGTCCAGTCCAG CAGATCACCATCACCTAAATTAATTGATTATGACATCCAAAGTGGCTTCTGGAGTCCCAAGTCGC CAGCAAAATCCCTAAATTAATTGATTATGACATCCAAAGTGGCTTCTGGAGTCCCAAGTCGC TTCAGTGGCAGTGGTCTGGGACCGAATTTACTCTCAATCAGCTCCCTGACGCTGATGACTT TGCCACTTATTACTGTCAGCAGTGGAGTAGGAATCACCTACACGTTTGGACAGGGACCAAGC TGGAATCAAA
721.	PM 99-F5 HL x I2C HL	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAASGFTFSDFMWVRQAPGKLEWSTIVSDGGSTVYRDSVK GRFTISRDNKNTLYLQMNSLTAEDTAIYCAKRGNSGYVMDAWGQGTITVTVSSGGSGGGGS GGGSDIQMTQSPSTLSASVGDRVITITCRASSSVTYMHVYQKPKSPKLLIYDTSKVASGVPSR FSGSGTEFTLTIISSLPDDFATYYCQWSRNSPYTFGQGTKLEIKSGGGSEVQLVESGGGLV QPGSLKLSCAASGFTFNKYAMNVRQAPGKLEWVRIRSKYNYATYVADSVKDRFTISRDDS KNTAYLQMNKLTEDTAVYCVRHGNGSYISWAYWGQTLTVTVSSGGSGGGSGGGSGGSGQT VVTQEPSLTVSPGGTTLTCGSSGTGAVTSGNYPNWVQKPKGQAPRGLIGGTFKFLAPGFARFSGS LLGKKAALTLSGVQPEDEAEYYCVLWYSNRWVFGGTKLTVL
722.	PM 86-F6 VL	artificial	aa	DIQMTQSPSTLSASVGKVTITCRASSSVTYMHVYQKPKAPKLLIYDTSKVASGVPSKFSGSG SGTEFTLTIISSLEPEDFATYYCQWSRNSPYTFGQGTKLEIK
723.	PM 86-F6 VL	artificial	nt	GACATCCAGATGACTCAGTCTCCATCAACCTGTCTGTCATCTGTGGGGAGAAAGTCAACATCAC CTGCCGTGCCAGCTCCAGTGTGACTTACATGCACTGTGTACAGCAGCAGCAAGCCAAAGCCCTA AATTATTGATTATGACACATCCAAAGTGGCTTCTGGAGTCCCAAGTCCGTTCAAGTGGAGTGGG TCTGGACCGGAATTTACTCTCAATCAGTCCCTGGAGCCTGAAGACTTGGCCACTTATTACTG TCAGCAGTGGAGTAGGAATCACCTACACGTTTGGACAGGGACCAAGCTGGAAATCAAA
724.	PM 86-F6 LCDR1	artificial	aa	RASSSVTYMH
725.	PM 86-F6 LCDR2	artificial	aa	DTSKVAS
726.	PM 86-F6 LCDR3	artificial	aa	QWSRNSPYT
727.	PM 86-F6 VH	artificial	aa	EVQLLESGGGLVQPGGSLKLSCAASGFTFSDFMWVRQAPGKLEWVATIVSDGGSTVYRDSVK GRFTISRDNKNTLYLQMDSLTSEDTAIYCAKRGNSGYVMDAWGQGTITVTVSS
728.	PM 86-F6 VH	artificial	nt	GAGTGCAGCTGCTCGAGTCTGGTGGAGGCTTAGTGCAGCCTGGAGGTCCTCAAACTCTCCTG TGACGCTCAGGATTCACCTTTCAGTACTTTTTCATGGCTGGTCCGCCAGGCTCCAGGGAAGG GGCTGGAGTGGTCCGAACCATTTGTTCTGATGGTGGTAGCACTTACTATCGGCACTCCGCTCAAG

					GGCCGTTTCACTATTCCAGAGATAATTCAAAAACACCCCTGTACCTGCAAAATGGACAGTGTGAC GTCTGAGGACACGGCATTATTACTGTGCAAGACCGGCAATTGGGGTACTATGTTATGATG CCTGGGTCAAGGAACACGGTCACCGTCTCCTCA
729.	PM 86-F6 HCDR1	artificial	aa		DFEMA
730.	PM 86-F6 HCDR2	artificial	aa		TIVSDGGSTYYRDSVKG
731.	PM 86-F6 HCDR3	artificial	aa		RNSGYVMDA
732.	PM 86-F6 HL	artificial	aa		EVQLLESGGGLVQPGGSLKLSAASGFTFSDFFWVRQAPGKGLEWVATIVSDGGSTYYRDSVK GRFTISRDNKNTLYIQMDSLTSEDTAIYYCARRNGSGYYVMDAWGQGTIVTVSSGGSGGGGS GGGSDIQMTQSPSTLSASVGEKVTITCRASSSVTYMHYQKPGKAPKLLIYDTSKVASGVPSR FSGSGSGTEFTLTISGLEPEDFATYYCQQWSRNSPYTFGQGTKLEIK
733.	PM 86-F6 HL	artificial	nt		GAGGTGACGCTGCTCAGTCTGGTGGAGGCTTAGTGACGCTGGAGGTCCTAAAACTCTCCTG TGCAGCCTCAGGATCACTTTTCACTGACTTTTTCATGGCTGGTCCGACGGCTCCAGGAAGG GGCTGAGTGGGTCCGAACCATTTTCTGATGGTGTAGTACCTACTATCGCGACTCCCTGAAG GGCCGTTTCACTATTCCAGAGATAATTCAAAAACACCCCTGACCTGCAATGGACAGTGTGAC GTCTGAGGACACGGCCATTATTACTGTGCAAGACGGGCAATTCGGGGTACTATGTTATGGATG CCTGGGTCAAGGAACACGGTACCGTCTCCTCAGTGTGTTCTGGCGGGGGGCTCC GGTGTGGTGTCTGACATCCAGATGACTCAGTCTCATCAACCCCTGTCTGATCTGTGGGGA GAAAGTCACCATCACTGCGTCCAGTCCAGTGTGACTTACATGACCTGTACACGACAGAAAGC CAGGCAAGCCCCATAATTGATTTATGACACATCCAAAGTGGCTTCTGGAGTCCCAAGTGGC TTCAGTGGCAGTGGTCTGGGACCGAATTTACTCTCAATCAGTCCCTGGAGCCCTGAAGACTT TGCCACTTATTACTGTCAGCAGTGGAGTAGGAACCTCAACCTACACGTTTGGACAGGGGACCAAGC TGGAAATCAAA
734.	PM 86-F6 HL x I2C HL	artificial	aa		EVQLLESGGGLVQPGGSLKLSAASGFTFSDFFWVRQAPGKGLEWVATIVSDGGSTYYRDSVK GRFTISRDNKNTLYIQMDSLTSEDTAIYYCARRNGSGYYVMDAWGQGTIVTVSSGGSGGGGS GGGSDIQMTQSPSTLSASVGEKVTITCRASSSVTYMHYQKPGKAPKLLIYDTSKVASGVPSR FSGSGSGTEFTLTISGLEPEDFATYYCQQWSRNSPYTFGQGTKLEIKSGGGSEVQLVESGGGLV QPGGSLKLSAASGFTFNKYAMNVRQAPGKGLEWVATIRSKYNNYATYYADSVKDRFTISRDDS KNTAYLQMNLLKTEDTAVYYCVRHGNGSYISYWAYWGQGTIVTVSSGGSGGGSGGGSGSQT VVTQEPSTLTVSPGGTIVTLTCSSTGAVTSGNYPNWWQKPGQAPRGLIGGKFLAPGTPARFSGS LLGGKAALTLSGVQPEDEAEYCYLVWSNRWVFGGKLTIVL
735.	PM 86-F6 HL x I2C HL	artificial	nt		GAGGTGACGCTGCTCAGTCTGGTGGAGGCTTAGTGACGCTGGAGGTCCTAAAACTCTCCTG TGCAGCCTCAGGATCACTTTTCACTGACTTTTTCATGGCTGGTCCGACGGCTCCAGGAAGG GGCTGAGTGGGTCCGAACCATTTTCTGATGGTGTAGTACCTACTATCGCGACTCCCTGAAG GGCCGTTTCACTATTCCAGAGATAATTCAAAAACACCCCTGACCTGCAATGGACAGTGTGAC GTCTGAGGACACGGCCATTATTACTGTGCAAGACGGGCAATTCGGGGTACTATGTTATGGATG CCTGGGTCAAGGAACACGGTACCGTCTCCTCAGTGTGGTGGTCTTGGCGGGGGGCTCC GGTGTGGTGGTCTCTGACATCCAGATGACTCAGTCTCATCAACCCCTGTCTGATCTGTGGGGA

736.	PM99-F5 HL-12C HL	artificial	nt

				CTGCTGGAGGCAAGGCTGCCCTCACCTCTCAGGGTACAGCAGGATGAGGCAGATATTA CTGTCTTCTATGGTACAGCAACCGTGGTGTTCGGTGAGGAACCAACTGACTGTCTTA
737.	5'PM3-VH-A-Xhol	artificial	nt	CCG GAT CTC GAG TCT GGC GGC GGA CTG GTG AAG CCT GGC GRC TCC CTG ARG CTG TCC TGT
738.	3'PM3-VH-B	artificial	nt	CCA GTA CAT GTA GTA GTC GGA GAA GGT GAA GCC GGA GRC GRY ACA GGA CAG CYT CAG GGA
739.	5'PM3-VH-C	artificial	nt	TAC TAC ATG TAC TGG RTC CGC CAG RCC CCT GRG AAG SGG CTG GAA TGG GTG KOC ATC ATC TCC GAC GGC (SEQ ID NO. 739)
740.	3'PM3-VH-D	artificial	nt	GGC GTT GTC CCG GGA GAT GGT GAA CCG GCC CTT GAT GAT GTC GGA GTA GTA GGT GTA GTA GCC GGC GTC GCA GAT GAT
741.	5'PM3-VH-E	artificial	nt	TCC CGG GAC AAC GCC AAG AAC ARC CTG TAC CTG CAG ATG ARC TCC CTG ARG KCC GAG GAC ACC GCC RTG TAC TAC TGC RCC CGG GGC
742.	3'PM3-VH-F-BstEII	artificial	nt	CGA TAC GGT GAC CAG GGT GCC CTG GCC CCA GTA ATC CAT GGC GCC GTG TCT CAG CAG AGG GAA GCC CCG GGY GCA GTA GTA
743.	5'PM4-VH-A-Xhol	artificial	nt	CTT GAT CTC GAG TCT GGC GCC GAA STG RWG RAG CCT GGC GCC TCC GTG AAG STG TCC TGC AAG GCC TCC GGC TAC
744.	3'PM4-VH-B	artificial	nt	CCA TTC CAG GCC CTG CYC AGG CSY CTG CUG CAS UCA GTT GAT GTC GAA GTA GGT GAA GGT GTA GCC GGA GGC CTT
745.	5'PM4-VH-C	artificial	nt	CAG GGC CTG GAA TGG ATS GGC GGC ATC TCC CCT GGC GAC GGC AAC ACC AAC TAC AAC GAG AAC TTC AAG
746.	3'PM4-VH-D	artificial	nt	AT GTA GGC GGT GGA GMT GGA CKT GTC TMT GGT CAK TGT GRC CYT GCC CTT GAA GTT CTC GTT GTA
747.	5'PM4-VH-E	artificial	nt	C TCC ACC GCC TAC ATS SAG CTG TCC CGG CTG ASA TCT GAS GAC ACC GCC GTG TAC TWC TGC GCC AGG GAC GGC
748.	3'PM4-VH-F-BstEII	artificial	nt	AGA CAC GGT CAC CGT GGT GCC CTG GCC CCA AGA GTC CAT GGC GTA GTA AGG GAA GTT GCC GTC CCT GGC GCA
749.	5'PM8-VH-A-Xhol	artificial	nt	CTT GAT CTC GAG TCC GGC SCT GAG STG RWG AAG CCT GGC GCC TCC GTG AAG RTG TCC TGC AAG GCC TCC GGC TAC
750.	3'PM8-VH-B	artificial	nt	CCA TTC CAG CMS CTG GCC GGG TKY CTG TYT CAC CCA GTG CAT CAC GTA GCC GGT GAA GGT GTA GCC GGA GGC CTT GCA
751.	5'PM8-VH-C	artificial	nt	CCC GGC CAG SKG CTG GAA TGG ATS GGC TAC ATC AAC CCT TAC AAC GAC GTG ACC CCG TAC AAC GGC AAG TTC AAG
752.	3'PM8-VH-D	artificial	nt	TTC CAT GTA GGC GGT GGA GGM GKA CKT GTC KCT GGT AAK GGT GRC TYT GCC CTT GAA CTT GCC GTT GTA
753.	5'PM8-VH-E	artificial	nt	TCC ACC GCC TAC ATG GAA CTG TCC RGC CTG ASG TCT GAG GAC ACC GCC GTG TAC TAC TGC GCC AGG GGC

754.	3'PM8-VH-F-BstEII	artificial	nt	CGA TAC GGT GAC CAG AGT GCC TCT GCC CCA GGA GTC GAA GTA GTA CCA GTT CTC GCC CCT GGC GCA GTA GTA
755.	5'PM3-VL-A-SacI	artificial	nt	CTT GAT GAG CTC CAG ATG ACC CAG TCC CCC ARS TYC MTG TCC RCC TCC GTG GGC GAC AGA GTG ACC
756.	3'PM3-VL-B	artificial	nt	GCC GGG CTT CTG CTG AWA CCA GGC CAC GTT GGT GTC CAC GTT CTG GGA GGC CTT GCA GGT GAY GGT CAC TCT GTC GCC
757.	5'PM3-VL-C	artificial	nt	CAG CAG AAG CCC GGC MAG KCC CCT AAG KCC CTG ATC TAC TCC GCC TCC TAC CGG TAC TCT
758.	3'PM3-VL-D	artificial	nt	CAG GGT GAA GTC GGT GCC GGA CYC GGA GGC GAA CCG GKM AGG CAC GYC AGA GTA CCG GTA GGA
759.	5'PM3-VL-E	artificial	nt	ACC GAC TTC ACC CTG ACC ATC TCC ARC STG CAG YCT GAG GAC YTC GCC RMG TAC TWC TGC CAG CAG TAC GAC
760.	3'PM3-VL-F- BsiWI/Spel	artificial	nt	CGA GTA ACT AGT CGT ACG CTT GAT TTC CAG CTT GGT CCC TCC GCC GAA GGT GTA AGG GTA GGA GTC GTA CTG CTG GCA
761.	5'PM4-VL-A-SacI	artificial	nt	CTT GAT GAG CTC GTG ATG ACC CAG TCC CCC CTG TCC CTG CCT GTG AYC CTG GGC SAM CMG GCC TCC ATC TCC TGC CGG
762.	3'PM4-VL-B	artificial	nt	AAA CCA GTG CAG GTA GGT ATT GCC GTT GGA GTG CAC CAG GGA CTG GGA GGA CCG GCA GGA GAT GGA GGC
763.	5'PM4-VL-C	artificial	nt	ACC TAC CTG CAC TGG TTT CWG CAG ARG CCT GGC CAG TCC CCT ARG CKG CTG ATC TAC ACC GTG TCC AAC CGG
764.	3'PM4-VL-D	artificial	nt	CAG GGT GAA GTC GGT GCC GGA GCC GGA CCG AGA GAA CCT GTC AGG CAC GCC GGA GAA CCG GTT GGA CAC GGT
765.	5'PM4-VL-E	artificial	nt	GGC ACC GAC TTC ACC CTG AAG ATC TCC CGG GTG GAG GCC GAA GAT STG GGC GTG TAC TWT TGC TCC CAG TCC ACC
766.	3'PM4-VL-F- BsiWI/Spel	artificial	nt	ACT CAG ACT AGT CGT ACG CTT GAT TTC CAG CTT GGT CCC TCC GCC GAA GGT AGG CAC GTG GGT GGA CTG GGA GCA
767.	5'PM8-VL-A-SacI	artificial	nt	CTT GAT GAG CTC GTG ATG ACC CAG TCT CCA SYC TCC CTG SCT GTG ACT CTG GGC CAG CSG GCC TCC ATC TCT TGC CGG
768.	3'PM8-VL-B	artificial	nt	CCA GTG CAT GAA GGT GTT GTC GTA GGA GTC GAT GGA CTC GGA GGC CCG GCA AGA GAT GGA GGC
769.	5'PM8-VL-C	artificial	nt	ACC TTC ATG CAC TGG TWT CAG CAG ARG CCT GGC CAG YCT CCT MRC CKG CTG ATC TWC CGG GCC TCT ATC CTG GAA
770.	3'PM8-VL-D	artificial	nt	CAG GGT GAA GTC GGT GCC GGA GCC AGA GCC GGA GAA CCG GKC AGG GAY GCC GGA TTC CAG GAT AGA GGC CCG
771.	5'PM8-VL-E	artificial	nt	ACC GAC TTC ACC CTG AMA ATC TMC CST GTG GAG GCC GAS GAC GTG GSC RYC TAC TAC TGC CAC CAG

772.	3'PM8-VL-F- BsiWI/SpeI	artificial	nt	ACT CAG ACT AGT CGT ACG CTT GAT TTC CAG CTT GGT CCC TCC GCC GAA GGT GTA AGG GTC CTC GAT GGA CTG GTG GCA GTA GTA
773.	PM84D7-H	artificial	aa	QVQLVQSGAEVKKPGASVKLSCKASGYTFTYFDINWVRQAPEQGLEWMGGISPGDGN TNYNENFKGRVMTIDTSSSTAYIELSRLTSDDTAVYYCARDGNFPYYAMDSWGQGT VTSS
774.	PM84D7-HCDR1	artificial	aa	YFDIN
775.	PM84D7-HCDR2	artificial	aa	GISPGDGN TNYNENFKG
776.	PM84D7-HCDR3	artificial	aa	DGNFPYYAMDS
777.	PM84D7-H	artificial	nt	CAGGTGCAGCTGCTCCAGTCTGGCGCCGAAGTGAAGAGCCTGGCGCCTCCGTGA AGCTGTCCTGCAAGGCCTCCGGCTACACCTTACCTACTTCGACATCAACTGGGTG CGCAGGGCCCTGAGCAGGGCTGGAATGGATGGCGGCATCTCCCTGGCGAC GGCAACACCAACTACAACGAGAACTTCAAGGGCAGGTCACATGACCATAGACAC GTCCAGCTCCACCGCTACATCGAGCTGTCCGGCTGACATCTGACGACACCGCC GTGTACTACTGCGCCAGGACGGCAACTTCCCTTACTACGCCATGGACTCTTGGGG CCAGGGCACCCAGGTGACCGTCTCCTCA
778.	PM84D7-L	artificial	aa	DIVMTQSPLSLPVTLGQASISCRSSQSLVHSNGNTYLHWFQRRPGQSPKLLIYTVSNR FSGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPTFGGKLEIK
779.	PM84D7-LCDR1	artificial	aa	RSSQSLVHSNGNTYLH
780.	PM84D7-LCDR2	artificial	aa	TVSNRFS
781.	PM84D7-LCDR3	artificial	aa	SQSTHVPT
782.	PM84D7-L	artificial	nt	GACATCGTGATGACCCAGTCCCCCCTGTCCCTGCCTGTGACCCCTGGGCCAACAGG CCTCCATCTCCTGCCGGTCTCCAGTCCCTGGTGCACTCCAACGGCAATACCTAC CTGCACCTGTTTCAGCAGAGGCCTGGCCAGTCCCTAAGCTGCTGATCTACACCGT GTCCAACCGGTTCTCCGGCTGCCTGACAGGTTCTCTGGCTCCGGCTCCGGCACCC GACTTCACCCCTGAAGATCTCCGGGTGGAGGCCGAAGATGTGGCGTGTAATT GCTCCAGTCCACCCACGTGCCTACCTTCGGCGGAGGACCAAGCTGGAATCAA G
783.	PM84D7-HL	artificial	aa	QVQLVQSGAEVKKPGASVKLSCKASGYTFTYFDINWVRQAPEQGLEWMGGISPGDGN TNYNENFKGRVMTIDTSSSTAYIELSRLTSDDTAVYYCARDGNFPYYAMDSWGQGT VTSSGGGGGGGGGGSDIVMTQSPLSLPVTLGQASISCRSSQSLVHSNGNTY LHWFQRRPGQSPKLLIYTVSNRFSQVDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQ STHVPTFGGKLEIK
784.	PM84D7-HL	artificial	nt	CAGGTGCAGCTGGTCCAGTCTGGCGCCGAAGTGAAGAGCCTGGCGCCTCCGTGA AGCTGTCCTGCAAGGCCTCCGGCTACACCTTACCTACTTCGACATCAACTGGGTG CGCAGGGCCCTGAGCAGGGCCTGGAATGGATGGCGGCATCTCCCTGGCGAC GGCAACACCAACTACAACGAGAACTTCAAGGGCAGGTCACATGACCATAGACAC

785.	PM84D7 HL x I2C HL	artificial	aa	<p> GTCCAGCTCCACCGCCTACATCGAGCTGTCCCGGCTGACATCTGACGACACCGCC GTGTA TACTGCGCAGGAGGCAACTTCCCTTACTACGCCATGACTCTTGGG CCAGGCAACACCGGTGACCGTCTCCTCAGGTGGTGGTCTTCTGGCGCGCGG CTCGGGTGGTGGTCTGACATCGTATGACCCAGTCCCCCTGTCCCTGCCGTG TGACCTGGGCAACAGGCTCCATCTCCTGCCGTCTCCAGTCCCTGGTGCA CTCAACGGCAATACCTACCTGCACTGGTTTTCAGAGAGGCTGGCCAGTCCCCTA AGCTGCTGATCTACACCGTGTCCAACCGGTTCTCCGGCTGCTGACAGGTTCTCT GGCTCCGGCTCCGGCACCGACTTCACTGAAGATCTCCGGGTGGAGGCCGAAG ATGTGGCGGTGACTATTGCTCCAGTCCACCCACGTGCTACCTTCGGCGGAGG GACCAAGCTGGAATCAAG </p> <p> QVQLVQSGAEVKKPGASVKLSCKASGYTFTYFDINWVQAPEQGLEWMGGISPGDGN TNYNENFKGRVTMTIDTSSTAYIELSRLTSDDTAVYCARDGNFPYAMDSWGGTT VTVSSGGGGGGGGGGSDIVMTQSPVLTGQQASISCRSSQSLVHSNGNTY LHWFQRPQSPKLLIYTVSNRFSVPDRFSGSGSDFTLKISRVEAEDVGVYCSQ STHVPTFGGKLEIKSGGGSEVQLVESGGGLVQPGSLKLSCAASGFTFNKYAMN WVRQAPGKLEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDT AVYYCVRHGNFNSYISYWAYWGQGLTVTVSSGGGGGGGGSGGSGTQVTVQEP SLTVSPGGTVTLTCSSTGAVTSGNYPNWWQKPGQAPRGLIGTKFLAPGTPARFSG SLLGGKAALTLGSGVQPEDEAEYCVLWYSNRWVFGGKLTVL </p> <p> CAGGTGCAGCTGGTCCAGTCTGGCGCCGAAGTGAAGAAGCCTGGCGCCTCCGTGA AGCTGTCTTGCAGGCGCTCCGGCTACACCTTACCTACTTCCACATCAACTGGGTG CGGACGGCGCTGAGCAGGCGCTGGAATGATGGCGGCGATCTCCCTGGCGAC GGCAACACCAACTACAACGAGAACTTCAAGGGCAGGTCACATGACCATAGACAC GTCCAGCTCCACCGCTACATCGAGCTGTCCGGCTGACATCTGACGACACCGCC GTGTACTACTGCGCCAGGACGGCAACTTCCCTTACTACGCCATGGAATCTTGGGG CCAGGGCACCGGTGACCGTCTCCTCAGGTGGTGGTGGTCTGGCGCGCGGG CTCGGGTGGTGGTCTGACATCGTATGACCCAGTCCCGCTGCTCCCTGCTGCTG TGACCTGGGCAACAGGCTCCATCTCCTGGCGTCTCCAGTCCCTGGTGCA CTCAACGGCAATACCTACCTGCACTGGTTTCAGCAGAGGCTGGCCAGTCCCCTA AGCTGCTGATCTACACCGTGTCCAACCGGTTCTCCGGGTGCTGACAGGTTCTCT GGCTCCGGCTCCGGCACCGACTTCACTGAAGATCTCCGGGTGGAGGCCGAAG ATGTGGCGGTGACTATTGCTCCAGTCCACCCACGTGCTACCTTCGGCGGAGG GACCAAGCTGGAATCAAGTCCGGAGGTGGTGGATCCGAGGTGCAGTGGTCCGAG TCTGGAGGAGGATTGGTGACCGCTGGAGGTGATTGAACCTCTCATGTGCAGCTC TGGATTACCTTCAATAAGTACGCCATGAAGTGGTGGTCCGCGAGGCTCCAGGAAGG GTTGGAAATGGGTGCTCGCATAGAAGTAAATATAATAATTATGCAACATATTATGC </p>
786.	PM84D7 HL x I2C HL	artificial	nt	

				CGATTGAGTGAAGACAGGTTACCATCTCCAGAGATGATTCAAAAACACTGCCTA TCTACAAATGAACAACCTGAAACACTGAGGACACTGCCGTGTAAGTGTGAGACA TGGGAACCTCGGTAATAGCTACATATCCTACTGGCTTACTGGGCAAGGGACTC TGGTCAACCGTCTCCTCAGGTGGTGGTCTGCGGCGGCGGCTCCGGTGGTG GTGGTCTCAGACTGTTGTGACTCAGGAACCTTCACTACCGTATCACCTGGTGA ACAGTCACACTCACTTGTGGTCTCCTGACTGGGCTGTACATCTGGCAACTACCC AACTGGGTCCAAACAAACAGGTACGACCCCGTGTCTAATAGTGGGACTA AGTTCCTCGCCCCGGTACTCCTGCCAGATTCTCAGGCTCCCTGCTGGAGGCAAG GCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGAGAAATATTACTGTGT TCTATGGTACAGCAACCGCTGGTGTTCGGTGGAGGAACCAACTGACTGTCTTA QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMYWVRQAPGKGLEWVAISDGGYY TYYSDIKGRFTISRDNKNNLYLQMNSLRAEDTAVYYCARGFPLLRHGAMDYWGQGT LVTSS
787.	PM76A9-H	artificial	aa	
788.	PM76A9-HCDR1	artificial	aa	DYYMY
789.	PM76A9-HCDR2	artificial	aa	IISDGGYYTYYSIIKIG
790.	PM76A9-HCDR3	artificial	aa	GFPLLRHGAMDY
791.	PM76A9-H	artificial	nt	CAGGTGCAGCTGGTCGAGTCTGGCGGCGGACTGGTGAAGCCTGGCGGCTCCCTG AGCGTGTCTCTGCGCCCTCCGGCTTCACTTCCGACTACTACATGATGATGGGT CCGCCAGGCCCTGGGAAGGGCTGGAATGGGTGGCCATCATCTCCGACGGCGG CTACTACACTACTACTCCGACATCATCAAGGGCGGTTACCATCTCCCGGGACA ACGCCAAGAACAACTGTACCTGCAGATGAATCCCTGAGGGCCGAGGACACCGC CGTGTACTACTGCGCCCGGGCTTCCCTCTGCTGAGACACGGCGGCGCATGGATTAC TGGGGCCAGGGCACCCCTGGTCACCGTCTCCTCA
792.	PM76A9-L	artificial	aa	DIQMTQSPSSLSASVGDRTTITCKASQNVDTNVAWYQQKPKGQAPKSLIYSASRYSDV PSRFSGSASGTDFTLTISSVQSEDFATYCCQQYDSYPYTFGGGTKEIK
793.	PM76A9-LCDR1	artificial	aa	KASQNVDTNVA
794.	PM76A9-LCDR2	artificial	aa	SASYRYS
795.	PM76A9-LCDR3	artificial	aa	QQYDSYPYT
796.	PM76A9-L	artificial	nt	GACATCCAGATGACCCAGTCCCCAGCTCCCTGTCCGCCCTCCGTGGCGGACAGAG TGACCATCACCTGCAAGGCCCTCCAGAACGTTGGACACCAACGTTGGCTGGTATCA GCAGAGCCCCGGCCAGGCCCTAAGTCCCTGATCTACTCCGCCCTCTACCCGTAC TCTGACGTGCTTCCCGGTTCTCCGGCTCCCGCTCCGGCACCGACTTCACCCCTGA CCATCTCCAGCGTGCAGTCTGAGGACTTCGCCACGTAATCTGCGCAGCAGTACGAC TCTACCCCTTACACCTTCGGCGGAGGGACCAAGCTGGAATCAAG
797.	PM76A9-HL	artificial	aa	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYYMYWVRQAPGKGLEWVAISDGGYY TYYSDIKGRFTISRDNKNNLYLQMNSLRAEDTAVYYCARGFPLLRHGAMDYWGQGT L

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801.	PM76A9-H codon optimized	artificial	nt		
802.	PM76A9-L codon optimized	artificial	nt		GACATCCAGATGACCCAGTCCCCTCCCTCCCTGCTGCCCTCCGTGGCGACAGAT GACCATACATGCAAGGCCCTCCAGAACGTGGACACCAACGTGGCATGGTATCAG CAGAAGCCAGGCCAGGCCCTAAGTCCCTGATCTACTTGCCTCCTACCCGTACTC CGAGTGCCCTCCAGGTCTCTGGCTCCGCCCTTGGCACCCGACTTCACCCGTACCA TCTCTCCGTGCAGTCCGAGGACTTCGCTACCTACTACTGCGCAGCTACGACTCC TACCCCTACACCTTCCGGCGGAGGCACCAAGCTGGAATCAAG
803.	PM76A9-HL codon optimized	artificial	nt		CAGGTGCAGCTGGTGCAGTCTGGCGCGGACTGGTCAAGCCTGGCGGCTCCCTG AGACTGTCTTGGCGTCCCTCCGGCTTCACTTCTCCGACTACTACATGTACTGGT CCGCCAGGCTCCTGGCAAGGACTGGAATGGTGGCCATCATCTCCGACGGCGG CTACTACACCTACTACTCCGACATCATCAAGGGCCGGTTACCATCTCCAGGGACA ACGCTAAGAACAACCTGTACCTGCAGATGAACCTCCCTGAGGCCGAGGACACCGC CGTGTACTACTGCGCCAGGGGCTTCCCACTGCTGAGACACGGCGCCATGGATTAC

<p>TGGGGCCAGGCAACCTGGTACAGTGTCTCTGCGGAGGCGGAAGTGGAGGC GGAGGAAGCGAGGCGGGGATCCGACATCCAGATGACCCAGTCCCATCCTCC TGCTGCCCTCCGTGGCGACAGAGTACCATCACATGCAAGGCTCCAGAACGT GGACCAACGTTGGCATGGTATCAGCAGAACCCAGGCCCTAAGTCCCTG ATCTACTGCTCTACCGGTACTCCGACGTGCCCTCCAGTCTCTGGTCCGC CTCTGGCACCAGTTCACCTGACCATCTCTCCGTGAGTCCGAGGACTTCGCTA CCTACTACTGCGCAGTACGACTCCTACCCTTACACCTTCGCGGAGGCACCAAG CTGGAATCAAG</p>				
<p>CAGGTGACGCTGGTCGAGTCTGGCGGCGGACTGGTCAAGCCTGGCGCTCCCTG AGACTGTCTTGGCTGCTCCGGCTTCACTTCTCCGACTACTACTGTTGGGT CCGCCAGGCTCCTGGCAAGGACTGGAATGGTGGCCATCATCTCCGACGGCGG CTACTACACTACTCTCCGACATCATCAAGGGCCGTTCACTCTCCAGGGACA ACGCTAAGAACAACTGTACCTGCAGATGAATCCCTGAGGGCCGAGACACCGC CGTGTACTACTGCGCAGGGCTTCCCACTGCTGAGACACGGCGCCATGGATTAC TGGGGCCAGGCAACCTGGTACAGTGTCTCTGCGGAGGCGGAAGTGGAGGC GGAGGAAGCGGAGGCGGGGATCCGACATCCAGATGACCCAGTCCCATCCTCC TGCTGCCCTCCGTGGCGACAGAGTGACCATCACATGCAAGGCTCCAGAACGT GGACCAACGTTGGTATCAGCAGAACCCAGCGAGGCCCTAAGTCCCTG ATCTACTGCTCTACCGGTACTCCGACGTGCCCTCCAGTCTCTGGTCCGC CTCTGGCACCAGTTCACCTGACCATCTCTCCGTGCAGTCCGAGGACTTCGCTA CCTACTACTGCCAGAGTACGACTCCTACCTTACACCTTCGCGGAGGCACCAAG CTGGAATCAAGTCCGGCGAGGGGCTCTGAAGTGCAGTGGTGGAAAGCGGA GGGGACTGGTGCAGCCCGGGGAAGTCTGAAGCTGTCTGTGCCCGCAGCGGC TTTACCTTCAACAAGTACGCCATGAATGGTCCGACAGGCCCCAGGGAAGGCCT GGAATGGGTGGCAGGATCCGGTCCAGTACAACAACTACGCCACTACTACGCT GACTCCGTGAAGGACAGATTCAACATCAGCGGGAGACTCTAAGAACACCGCCTA TCTGCAGATGAACAACCTGAAACCGAGGATACAGCTGTACTATTGTGGGGC ACGGCAACTTCGGCAACTCTACATCTCTACTGGCCCTATTGGGACAGGGAACA CTGGTACCGGTGTAGCGGAGGTGGCGGAAGTGGGGAGGCGGATCTGGCGGT GGCGGATCCAGACCGTGGTCAACCCAGGAACCTTCCCTGACCGTCTCCCGAGCG GCACCGTGACCTGACCTGGCTCTCTACCGCGCTGTGACCTCCGGCAACTA CCCTAACTGGGTGCAGCAGAAACCCGACAGGCTCTAGAGGCTGTATGGCGGC ACCAAGTTTCTGGCCCTGGCACCCCTGCCAGATTCTCCGGTCCCTGCTGGGAG GCAAGGCCGCTCTGACCCCTGTCTGGCTGCAGCCTGAGGACGAGGCCGAGTACTA CTGTGTGTGTGTTACTCCAACAGATGGGTGTTCCGAGGCGGCACAAAGCTGACC GTGCTG</p>	nt	artificial	PM76A9 HL x I2C HL_ codon optimized	804.

805.	PM76B10-H	artificial	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSDYYMYVWRQAPGKGLEWVAISDGGYY TYYSDIKGRFTISRDNAKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMDYWGQGTL VTSS
806.	PM76B10-HCDR1	artificial	aa	DYYMY
807.	PM76B10-HCDR2	artificial	aa	IISDGGYYTYYSDIKIG
808.	PM76B10-HCDR3	artificial	aa	GFPLLRHGAMDY
809.	PM76B10-H	artificial	nt	CAGGTGCAGCTGGTCGAGTCTGGCGGGGAGCTGGTGAAGCCTGGCGAGTCCCTG AGGCTGTCTGTGCCGCTCCGGCTTCACTTCCGACTACTACATGACTGGGT CCGCCAGGCCCTGGGAAGGGCTGGAATGGTGGCCATCATCTCCGACGGCGG CTACTACACTACTCTCCGACATCATCAAGGGCCGTTACCATCTCCCGGACA ACGCCAAGAACAGCCTGTACCTGCAGATGAATCCCTGAAGCCGAGGACACCGC CGTGTACTACTGCCCGGGCTTCCCTCTGCTGAGACACGGCGCCATGGATTAC TGGGGCCAGGGCACCTGGTCACCGTCTCCTCA
810.	PM76B10-L	artificial	aa	DIQMTQSPSSLSASVGDRTITCKASQNVDTNVAWYQQKPGQAPKSLIYSASYRSDV PSRFGSASGIDFTLTISVQSEDFATYCCQYDSYPYTFGGGTKLEIK
811.	PM76B10-LCDR1	artificial	aa	KASQNVDTNVA
812.	PM76B10-LCDR2	artificial	aa	SASYRYS
813.	PM76B10-LCDR3	artificial	aa	QYDSYPYT
814.	PM76B10-L	artificial	nt	GACATCCAGATGACCCAGTCCCCAGCTCCCTGTCGGCTCCGTGGCGGACAGAG TGACCATCACCTGCAAGGCTCCAGAACGTGGACACCAACGTGGCCTGGTATCA GCAGAAGCCCGGAGGCCCCCTAAGTCCCTGATCTACTCCGCTCCCTACCGGTAC TCTGACGTGCCCTCCCGGTTCTCCGGCTCCGCTCCGGCACCGACTTCAACCTGA CCATCTCCAGCGTGCAGTCTGAGGACTTCGCCACGTACTGCGCAGCAGTACGAC TCCTACCCCTTACACCTTCGGCGGAGGACCAAGCTGGAATCAAG
815.	PM76B10-HL	artificial	aa	QVQLVESGGGLVKPGESLRLSCAASGFTFSDYYMYVWRQAPGKGLEWVAISDGGYY TYYSDIKGRFTISRDNAKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAMDYWGQGTL VTSSGGGGGGGGGGSDIQMTQSPSSLSASVGDRTITCKASQNVDTNVAWY QQKPGQAPKSLIYSASYRSDVPSRFGSASGIDFTLTISVQSEDFATYCCQYDSYP YTFGGGTKLEIK
816.	PM76B10-HL	artificial	nt	CAGGTGCAGCTGGTCGAGTCTGGCGGGGAGCTGGTGAAGCCTGGCGAGTCCCTG AGGCTGTCTGTGCCGCTCCGGCTTCACTTCCGACTACTACATGACTGGGT CCGCCAGGCCCTGGGAAGGGCTGGAATGGTGGCCATCATCTCCGACGGCGG CTACTACACTACTCTCCGACATCATCAAGGGCCGTTACCATCTCCCGGACA ACGCCAAGAACAGCCTGTACCTGCAGATGAATCCCTGAAGCCGAGGACACCGC CGTGTACTACTGCCCGGGCTTCCCTCTGCTGAGACACGGCGCCATGGATTAC TGGGGCCAGGGCACCTGGTCACCGTCTCCTCAGTGGTGGTCTGGCGGC

817.	PM76B10 HL x I2C HL	artificial	aa
818.	PM76B10 HL x I2C HL	artificial	nt

(20) $\text{inf } f = \inf \{f(x) : x \in X\}$

		HL codon optimized			<p>GACTGTCTTGGCGTGCTCCGGCTTACCTTCTCCGACTACTACATGACTGGGTC CGCCAGGCTCCTGGCAAGGACTGGAATGGTGGCCATCATCTCCGACGGCGCT ACTACACCTACTACTCCGACATCATCAAGGGCCGTTACCATTCTCCAGGACAAC GCCAAGAACTCCCTGTACCTGCAGATGAATCCCTGAAGCCCGAGACACCCCGG TGTAATACTGCCAGGGCTTCCCATGCTGAGACACGGCCCATGGATTACTG GGCCAGGGCACCTGGTACAGTGTCTCTGGCGAGCGGAAGTGGAGCGGG AGGAAGCGGAGGGCGGATCCGACATCCAGATGACCCAGTCCCATCTCCCTG TCTGCCTCCGTGGCGACAGAGTGACCATCACATGCAAGGCCCTCCAGAACGTGG ACACCAACGTGGCATGGTATCAGCAGAAAGCCAGGCCAGGCCCTAAGTCCCTGAT CTACTCTGCCCTACCGTACTCCGACGTGCCCTCCAGGTTCTCTGGCTCCGCT CTGGCACCGACTTCAACCTGACCATCTCTCCGTGCAGTCCGAGGACTTCGCTACC TACTACTGCCAGCAGTACGACTCTACCTTACACCTTCCGCGGAGGACCAAGCT GGAAATCAAGTCCGGCGGAGGGGCTCTGAAGTGCAGCTGTCTGTCCCGCAGCGCTT GGGACTGGTGCAGCCCGGGGAAGTCTGAAGTGTCTGTCAGCGCCAGGAAAGCGCTT ACCTTCAACAAGTACGCCATGAATTGGTCCGACAGGCCCGAGGAAAGCGCTGG AATGGTGGCACGGATCCGTCCTCAAGTACAACACTAGCCACCTACTACGCTGAC TCCGTGAAGGACAGATTACCATCAGCGGACGACTTAAGAACACCGCCTATCT GCAGATGAACAACCTGAAACCGAGGATACAGCTGTACTATTGTGTCCGCGACG GCAACTTCGGCAACTCTACATCTCTACTGGGCTATTGGGACAGCGGAACACTG GTCACCGTGTCTAGCGGAGGTGGCGAAGTGGGGAGGCGGATCTGGCGGTGGC GGATCCAGACCGTGGTCAACCGAAGCTTCCCTGACCGTCTCCCGAGCGGCA CCGTGACCTGACCTGTGGCTCTCTACCGCGCTGTGACCTCCGGCAACTACCC TAACTGGGTGCAGCAGAAACCCGACAGGCTCTTAGAGGCTGATCGGCGGCACC AAGTTTCTGGCCCTGGCACCCCTGCCAGATTCTCCGGCTCCCTGCTGGGAGGCA AGGCCGCTCTGACCTGTCTGGCGTGCAGCTGAGGACGAGGCCGAGTACTACTG TGTGCTGTGGTACTCCACAGATGGGTGTCGGAGGCGGACACAAAGCTGACCGTG CTG</p>
823.	PM34C7-H		artificial	aa	<p>EVQLLEQSGAELVKPGASVKLSCTASGFNIKDTYMDWVKORPEQGLEWIARDPANGD SKYDPKFQGGKATITADTSSNTAYLQLSSLTSEDYAVYYCARGGMIWYFDVWGQGT VSS</p>
824.	PM34C7-HCDR1		artificial	aa	DTYMD
825.	PM34C7-HCDR2		artificial	aa	RIDPANGDSKYDPKFQG
826.	PM34C7-HCDR3		artificial	aa	GGMWYFDV
827.	PM34C7-H		artificial	nt	<p>GAGGTGCAGCTGCTCGAGCAGTCTGGGGCAGAGCTTGTGAAGCCAGGGGCCCTCA GTCAAGTTGTCTGCACAGCTTCTGGCTTCAACATTAAAGACACCTATATGGACTGG GTGAAGCAGAGGCTGAACAGGGCCCTGGAATGGATTGCAAGGATTGATCCTCGGA</p>

					ATGGTGATAGTAAATATGACCCGAAATTCAGGGCAAGGCCACTATAACAGCAGAC ACATCCTCCAACACAGCCTACCTGCAGCTCAGCAGCCTGACATCTGAGGACACTGC CGTCTATTATTGTGTAGAGCGGGATGATATGGTACTTCGATGTCTGGGCCAAG GGACCACGGTCACCGTCTCTCTCA
828.	PM34C7-L	artificial	aa		ELVLTQSPTTMAASPGKIIITCSASSISSNYLHWYQQKPGFSPKLLIYRTSNLASGVP ARFSGSGSGTSYSLTIGTMEAEADVATYYCQQGSSLPYTFGGGKLEIK
829.	PM34C7-LCDR1	artificial	aa		SASSISSNYLH
830.	PM34C7-LCDR2	artificial	aa		RTSNLAS
831.	PM34C7-LCDR3	artificial	aa		QQGSSLPYT
832.	PM34C7-L	artificial	nt		GAGCTCGTGCTCACCAGTCTCCAACCACCACATGGCTGCATCTCCCGGGGAGAAGA TCACTATCACCCTGCAGTGCCAGCTCAAGTATAAGTCCAAATTGCAATTGGTATC AGCAGAAAGCCAGGATCTCCCTAAACTCTTGATTATAGGACATCCAATCTGGCTT CTGGAGTCCCAGCTCGCTTCAGTGGCAGTGGTCTGGACCTCTTACTCTCTCACA ATTGGCACCATGGAGGCTGAAGATGTTGCCACTTACTACTGCCAGCAGGGTAGTAG TTTACCGTACACGTTCCGAGGGGGACCAAGCTTGAGATCAAA
833.	PM34C7-HL	artificial	aa		EVQLLEQSGAELVKPGASVKLSCTASGFNIKDTYMDWVKRPEQGLEWRIADPANGD SKYDPKFQGKATITADTSSNTAYLQLSSLTSEDYAVYCARGGMIWYFDVWGQGT VSSGGGSGGGGGGSELVLTQSPPTMAASPGKIIITCSASSISSNYLHWYQQK PGFSPKLLIYRTSNLASGVPARFSGSGSGTSYSLTIGTMEAEADVATYYCQQGSSLPYTF GGGKLEIK
834.	PM34C7-HL	artificial	nt		GAGGTGCAGCTGCTCGAGCAGTCTGGGGCAGAGCTTGTGAAGCCAGGGCCCTCA GTCAAGTTGTCCTGCACAGCTTCTGGCTTCAACATTAAAGACACCTATATGGACTGG GTGAAGCAGAGGCGCTGAACAGGGCCTGGAATGGATTGCAAGGATTGATCCTGCGA ATGGTGATAGTAAATATGACCCGAAATTCAGGGCAAGGCCACTATAACAGCAGAC ACATCCTCCAACACAGCCTACCTGCAGCTCAGCAGCCTGACATCTGAGGACACTGC CGTCTATTATTGTCTAGAGCGGGATGATATGGTACTTCGATGTCTGGGCCAAG GGACCACGGTCACCGTCTCCTCAGGTGGTGGTGGTCTGGCGGGCGGCTCCG GTGGTGGTGGTCTGAGCTCGTGTCTCAGCTCAGCTCAGCTCAGCTCAGCTCAGCTC CCCGGGGAGAAAGATCACTATCACCTGCAGTCCAGCTCAGCTCAGCTCAGCTCAGCT CTTGCAATTGGTATCAGCAGAACCCAGGATTCCTCCCTAAACTCTTGATTATAGGAC ATCCAATCTGGCTTCTGGAGTCCAGCTCGCTTCAAGTGGCAGTGGTCTGGGACCT CTTACTCTCTCACAATTGGCACCATGGAGGCTGAAGATGTTGCCACTTACTACTGCC AGCAGGGTAGTAGTTTACCGTACACGTTCCGAGGGGGACCAAGCTTGAGATCAAA
835.	PM34C7 HL x I2C HL	artificial	aa		EVQLLEQSGAELVKPGASVKLSCTASGFNIKDTYMDWVKRPEQGLEWRIADPANGD SKYDPKFQGKATITADTSSNTAYLQLSSLTSEDYAVYCARGGMIWYFDVWGQGT VSSGGGSGGGGGGSELVLTQSPPTMAASPGKIIITCSASSISSNYLHWYQQK

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				<p>ACTCCTAATTATAAGGTTTCTAACCGGTTCTCTGGGTCCAGACAGATTACGCGG CAGTGGTCAGGCACTGATTTACACTGAAATCAGCAGGTGAGGCTGAGGAT GTTGGGTTTACTACTGCTCTCAAAGTACACATGTTCCGTACACGTTTGCCAGGG GACCAAGCTGGAGATCAAA</p>
849.	PM49B9 HL x I2C HL	artificial	aa	<p>QVLVQSGAEVKKPGASVKLSCKASGYTFTYDINWVRQTPEQGLEWMGGISPGDGN TNYNENFKGRVTMTSDTSNAYMELSLRSDDTAVYCARDGNFPYYAMDSWQQG TTTVSSGGGGGGGGGGSDIVMTQPLSLPTLGDPAISCRSSQLSVYSGNT YLNWYQRPQSPRLIYKVSNNRFSVDPDRFSGSGSDFTLKISRVEAEDVGVYCS QSTHVPYTFGQGTKEIKSGGGSEVQLVESGGGLVQPGGSLKLSAASGFTFNKYA MNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNLLKT EDTAVYCVRHGNFNSYISYWAYWQQGLTVTVSSGGGGGGGGGGSGGQTVVT QEPSLTVSPGGTVTLTCSGSTGAVTSGNYPNWWQKPGQAPRGLIGGTFKFLAPGTPA RFSGLLGGKAAALTLGGVQPEDEAEYCYLVYSNRWVFGGKLTVL</p>
850.	PM49B9 HL x I2C HL	artificial	nt	<p>CAGGTGCAGCTGGTCCAGTCTGGCGCCGAAGTGAAGAAGCTGGCGCCTCCGTGA AGCTGTCTCTGCAAGGCTCCGGCTACACCTTCACTTCTCGACATCAACTGGGTG CGGCAGACGCGCTGAGCAGGCGCTGGAATGGATGGCGGCATCTCCCTGGCGAC GGCAACACCAACTACAACGAGAACTTCAAGGCGAGGTCACAATGACAGAGACAC GTCCAACTCACCGCTACATGGAGTGTCCGGCTGAGATCTGACGACACCGCC GTGTACTACTGGCCAGGACGGCAACTTCCCTTACTACGCCATGGAATCTTGGG CCAGGCGACCAAGGTACCGTCTCTCAGCTGGTGGTCTTGGCGGCGCGCG CTCCGGTGGTGGTCTGACGTCTGATGACTCAGACTCCACTCTCCCTGCCCG TCACCTTGAGACCGCGCTCCATCTCTGCAGGTCTAGTCAAAGCCTCGTATAC AGTAACGGAAACACCTACTTGAATTGGTATCAACAGAGGCCAGGCCAATCTCCAAG ACTCCTAATTATAAGGTTTCTAACCGGTTCTCTGGGTCCAGACAGATTACGCGG CAGTGGTTCAGGCACTGATTTCACTGAAATCAGCAGGTGGAGGCTGAGGAT GTTGGGTTTACTACTGCTCTCAAAGTACACATGTTCCGTACACGTTTGCCAGGG GACCAAGCTGGAGATCAATCCGAGGTGGTGGATCCGAGGTGCAGTGGTCGAG TCTGGAGGAGGATTGGTGCAGCTGGAGGTGATTGAAACTCTCATGTGCAGCCTC TGGATTCACTTCAATAAGTACGCCATGAAGTGGTCCGCCAGGCTCCAGGAAAGG GTTTGAATGGGTTGCTCGCATAGAAGTAATAATAATATGCAACATATTATGC CGATTCAAGTGAAGACAGGTTCAACATCTCCAGAGATGATTCAAAAACACTGCCTA TCTACAAATGAACAACCTGAAAACCTGAGGACACTGCCGTGTACTGTGTGAGACA TGGGAACCTTCGGTAATAGCTACATATCCTACTGGCTTACTGGGCCAAGGGACTC TGGTCACCGTCTCCTCAGGTGGTGGTGGTCTGGCGGGGGGCTCCGGTGGTG GTGGTTCTCAGACTGTTGTGACTCAGGAACCTTCACTACCGGTATCACCTGGTGA ACAGTCACACTCACTTGTGGCTCCTCGACTGGGCTGTACATCTGCCAACTACCC</p>

					AACTGGGTCCAACAAAACAGGTGAGGACCCCGTGGTCTAATAGTGGGACTA AGTTCCTCGCCCCCGGTACTCCTGCCAGATTCTCAGGCTCCCTGCTTGGAGGCAAG GCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAGAAATTACTGTGT TCTATGGTACAGCAACCGCTGGGTGTTCCGGTGGAGGAACCAACTGACTGTCTTA
851.	PM29G1-H	artificial	aa		QVQLVQSGAEVKKPGASVKLSCKASGYTFTYFDINWVRQTPAQGLEWMGGISPGDGN TNYNENFKGRVTMTDRDTSNSTAYMELSLRSDDTAVYYCARDGNFPYYAMDSWGQG TTVTVSS
852.	PM29G1-HCDR1	artificial	aa		YFDIN
853.	PM29G1-HCDR2	artificial	aa		GISPGDGN
854.	PM29G1-HCDR3	artificial	aa		TNYNENFKG
855.	PM29G1-H	artificial	nt		DGNFPYYAMDS CAGGTGCAGCTGGTCCAGTCTGGCGCCGGAAGTGAAGAAGCCCTGGCGCCTCCGTGA AGCTGTCTCTGCAAGGCCCTCGGCTACACCTTCACCTACTTCGACATCAACTGGGTG CGGCAGACGCCCTGAGCAGGGCCTGGAATGGATGGCGGCATCTCCCTGGCGAC GGCAACACCAACTACAACGAGAACTTCAAGGGCAGGTCACATGACCAGAGACAC GTCCAACCTCCACCGCTACATGGAGCTGCCGGCTGAGATCTGACGACACCGCC GTGTACTACTGGCGCAGGACGGCAACTTCCCTTACTACGCCATGGACTCTTGGGG CCAGGACCCAGGTCACCGTCTCCTCA
856.	PM29G1-L	artificial	aa		DVVMTQSPSLPVTLGEPAISCRSSQSLVSYNGNTYLHWYQQKPGQSPRLIYKVSN RFGVDPDRFSGSGSGTDFTLKISRVEAEDVGVYFCQSQSTHVPYTFGGQGTKLEIK
857.	PM29G1-LCDR1	artificial	aa		RSSQSLVSYNGNTYLH
858.	PM29G1-LCDR2	artificial	aa		KVSNRFS
859.	PM29G1-LCDR3	artificial	aa		SQSTHVPYT
860.	PM29G1-L	artificial	nt		GACGTCGTGATGACTCAGTCTCCACTCTCCCTGCCCCGTACCCCTGGAGAGCCGG CCTCCATCTCCTGCAGGTCTAGTCAAGCCCTCGTATACAGTAACGGAACACCTACT TGCATTGGTATCAACAGAAGCCAGGCCAATCTCCAAGACTCCTAATTTATAAGGTTT CTAACCGGTTCTCTGGGTCCAGACAGATTACGCGGCAGTGGTCAGGCACTGA TTTCACACTGAAATCAGCAGGGTGGAGGCTGAGGATGTTGGGGTTTATTTCTGCT CTCAAAGTACACATGTTCCGTACACGTTTGCCAGGGGACCAAGCTGGAGATCAAA
861.	PM29G1-HL	artificial	aa		QVQLVQSGAEVKKPGASVKLSCKASGYTFTYFDINWVRQTPAQGLEWMGGISPGDGN TNYNENFKGRVTMTDRDTSNSTAYMELSLRSDDTAVYYCARDGNFPYYAMDSWGQG TTVTVSSGGGGSGGGGGSDVMQSPSLPVTLGEPAISCRSSQSLVSYNGN TYLHWYQQKPGQSPRLIYKVSIRFSGVDPDRFSGSGSGTDFTLKISRVEAEDVGVYFC SQSTHVPYTFGGQGTKLEIK
862.	PM29G1-HL	artificial	nt		CAGGTGCAGCTGGTCCAGTCTGGCGCCGGAAGTGAAGAAGCCCTGGCGCCTCCGTGA AGCTGTCTCTGCAAGGCCCTCGGCTACACCTTCACCTACTTCGACATCAACTGGGTG CGGCAGACGCCCTGAGCAGGGCCTGGAATGGATGGCGGCATCTCCCTGGCGAC

863.	PM29G1 HL x 12C HL	artificial	aa	<p>GGCAACACCACTACAACGAGAACTTCAAGGGCAGGGTCACAAATGACCAAGACACAC GTCCAACCTCCACCGCTACATGAGCTGTCCCGGTGAGATCTGACGACACCGCC GTGTACTACTGCGCCAGGACGGCAACTTCCCTTACTACGCCATGGACTCTTGGGG CCAGGGCACCAAGTACCGTCTCCTCAGGTGGTGGTCTGCGCGCGCGG CTCCGGTGGTGGTCTGACGTCTGATGACTCAGTCTCCACTCTCCCTGCCCG TCACCCCTGGAGAGCCGCCCTCCATCTCCTGCAAGTCTAGTCAAAGCCTCGTATAC AGTAACGGAAACACCTACTTGCATTGGTATCAACAGAACCCAGGCCAATCTCCAAG ACTCCTAATTATAAGGTTCTAACCGGTTCTGCGGGTCCAGACAGATTCAAGCGG CAGTGGGTCAGGCACGTGATTTACACTGAAATCAGCAGGTTGAGGCTGAGGAT GTTGGGGTTATTTCTGCTCTCAAAGTACACATGTTCCGTACACGTTTGGCCAGGGG ACCAAGCTGGAGATCAAA</p> <p>QVQLVQSGAEVKKPGASVKLSCKASGYTFTYFDINWVRQTPEQGLWMGGISPGDGN TNYNENFKGRVTMTTRDTSNSTAYMELSLRSDDTAVYYCARDGNFPYYAMDSWGQG TTVTVSSGGGGGGGGGGSDVDVMTQSPSLPVTLPGLPISCRSSQSLVYSNGN TYLHWYQQKPGQSPRLIYKVSINRFSGVDPFSGSGSGTDFTLKISRVEAEDVGVYFC SQSTHVPYTFGGGTKLEIKSGGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYA MNWVRQAPGKGLWVARIKSYNNYATYYADSVKDRFTISRDDSKNTAYLQMNLLKT EDTAVYYCVRHGNFNSYISYWAYWGQGTLVTVSSGGGGGGGGGGGSGTQVWT QEPSTLVSPGGTIVLTGSSSTGAVTSGNYPNWNVQKPGQAPRGLIGGTFKLAPGTPA RFGSLLGGKAALTLGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL</p>
864.	PM29G1 HL x 12C HL	artificial	nt	<p>CAGGTGCAGCTGGTCCAGTCTGGCGCCGAAGTGAAGAGCCTGGCGCCTCCGTGA AGCTGTCTGCAAGGCCTCCGGCTACACCTTACCTACTTCGACATCAACTGGGTG CGGCAGACGCCTGAGCAGGGCCTGGAATGGATGGCGCGCATCTCCCTGGCGAC GGCAACACCAACTACAACGAGAACTTCAAGGGCAGGGTCACAAATGACCAAGACAC GTCCAACCTCCACCGCTACATGAGCTGTCCCGGTGAGATCTGACGACACCGCC GTGTACTACTGCGCCAGGACGGCAACTTCCCTTACTACGCCATGGACTCTTGGGG CCAGGGCACCAAGTCAACCGTCTCCTCAGGTGGTGGTCTGCGCGCGCGCGG CTCCGGTGGTGGTCTGACGTCTGATGACTCAGTCTCCACTCTCCCTGCCCG TCACCCCTGGAGAGCCGGCCTCCATCTCTGCAAGTCTAGTCAAAGCCTCGTATAC AGTAACGGAAACACCTACTTGCATTGGTATCAACAGAACCCAGGCCAATCTCCAAG ACTCCTAATTATAAGGTTCTAACCGGTTCTGCGGGTCCAGACAGATTCAAGCGG CAGTGGGTCAGGCACGTGATTTACACTGAAATCAGCAGGTTGAGGCTGAGGAT GTTGGGGTTATTTCTGCTCTCAAAGTACACATGTTCCGTACACGTTTGGCCAGGGG ACCAAGCTGAGATCAAAATCCGAGGTGGTGGATCCGAGGTGACGCTGGTGGT CTGGAGGAGGATTGGTGCAGCCTGGAGGGTCAATTGAACTCTCATGTGCAGCCTCT GGATTCACCTTCAATAAGTACGCCATGAAGTGGGTCCGCCAGGCTCCAGGAAAGGGG</p>

55	865.	PM29G1-H codon optimized	artificial	nt	<p>TTTGGAAATGGGTTGCTCGCATAGAAGTAAATATAATAATTATGCAACATATTATGCC GATTGAGTGAAAGACAGGTTACCATTCCAGAGATGATTCAAAAACACTGCCTAT CTACAATGAACAACATTGAAAACCTGAGGACACTGCCGTGACTACTGTGTGAGACAT GGAACTTCGGTAATAGCTACATATCCTACTGGCTTACTGGGCCAAGGACTCT GGTCACCGTCTCCTCAGGTGGTGGTCTGCGCGCGGCTCCGGTGGTGG TGGTTCTCAGACTGTTGTGACTCAGGAACCTTCACTCACCGTATCACCTGGTGGAA CAGTCACACTCACTTGTGGCTCCTCGACTGGGCTGTACATCTGGCAACTACCCA AACTGGGTCCAACAAAACCAGGTACAGGCACCCGCTGTCTAATAGGTGGACTAA GTTCTCGCCCCGGTACTCCTGCCAGATTCTCAGGCTCCCTGCTTGGAGGCAAG GCTGCCCTCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAAGATATTACTGTGT TCTATGGTACAGCAACCGCTGGTGTTCGGTGGAGGAACCAAACTGACTGTCCTA CAGGTGCAGCTGGTCCAGTCAGGCGCCGAAGTGAAGAAACCTGGCGCCTCTGTGA AGCTGTCTGCAAGGCCCTCCGGCTACACCTTCACTTCTCGACATCAACTGGGTC CGCCAGACCCCTGAGCAGGGCCTGGAATGGATGGCGGCATCTCCCTGGCGAC GGCAACACCAACTACAACGAGAACTTCAAGGCGAGAGTGACCATGACCAGGGACA CCTCTAACTCCACCGCTACATGGAACCTGTCGGCTGAGATCCGACGACACCGCC GTGTACTACTGCGCCAGGACGGCAACTTCCCTTACTACGCCATGGACTCTTGGG CCAGGGCACCACTGACAGTGTCTCTGCGCGCGGAGGAAGTGGAGGTGGAGG ATCTGGCGGAGCGGCTCCGATGTGGTATGACCCAGTCCCACTGTCCCTGGCT GTGACCCCTGGCGAGCGCTGCCTCCATCTCCTGCCGCTCCCTCCAGTCCCTGGTGT ACTCCAACGGCAATACCTACCTGCACTGCTGATCAGCAGAAAGCTGGCCAGTCCCT AGGCTGCTGATCTACAAGGTGTCCAAACCGGTTCTCCGGCGTCCCGACAGATTCTC</p>
50	866.	PM29G1-L codon optimized	artificial	nt	<p>GATGTGTCATGACCCAGTCCCCAGTGTCCCTGCTGTGACCCCTGGCGGAGCCTG CCTCCATCTCCTGCGGCTCCTCCAGTCCCTGCTGTGACTCCAACGGCAATACCTAC CTGCACTGGTATCAGCAGAGCCTGGCGAGTCCCTAGGCTGCTGATCTACAAGT GTCCAACCGGTTCTCCGGCGTGCCCGACAGATTCTCCGGCTCCGGCTCTGGCACC GACTTCACACTGAAGATCTCCAGGTGGAGGCTGAGGACGTGGCGGTGACTTCT GCTCCCAGTCCACCCACGTGCCCTACACCTTCGGACAGGGCACCAAGCTGGAAT CAAG</p>
45	867.	PM29G1-H codon optimized	artificial	nt	<p>CAGGTGCAGCTGGTCCAGTCAAGCGCCGAAGTGAAGAAACCTGGCGCCTCTGTGA AGCTGTCTGCAAGGCCCTCCGGCTACACCTTCACTTCACTTCCGACATCAACTGGGTC CGCCAGACCCCTGAGCAGGGCCTGGAATGGAATGGCGCGCATCTCCCTGGCGAC GGCAACACCAACTACAACGAGAACTTCAAGGCGAGAGTGACCATGACCAGGGACA CCTCTAACTCCACCGCTACATGGAACCTGTCGGCTGAGATCCGACGACACCGCC GTGTACTACTGCGCCAGGACGGCAACTTCCCTTACTACGCCATGGACTCTTGGG CCAGGGCACCACTGACAGTGTCTCTGCGCGCGGAGGAAGTGGAGGTGGAGG ATCTGGCGGAGCGGCTCCGATGTGGTATGACCCAGTCCCACTGTCCCTGGCT GTGACCCCTGGCGAGCGCTGCCTCCATCTCCTGCCGCTCCCTCCAGTCCCTGGTGT ACTCCAACGGCAATACCTACCTGCACTGCTGATCAGCAGAAAGCTGGCCAGTCCCT AGGCTGCTGATCTACAAGGTGTCCAAACCGGTTCTCCGGCGTCCCGACAGATTCTC</p>

868.	PM29G1 HL x l2C HL codon optimized	artificial	nt	<p>CGGCTCGGGCTCTGGCACCGAGCTTCAACATGAAGATCTCCAGGGTGGAGGCTGAG GACGTGGGCGGTACTTCTGCTCCAGTCCACCCACGTGCCCTACACCTTCGGACA GGCACCAAGCTGGAATCAAG</p> <p>CAGGTGCAGCTGGTCCAGTCAAGGCGCCGAAGTGAAGAAACCTGGCGCCTCTGTGA AGCTGTCTGCAAGGCCCTCGGCTACACCTTACACCTACCTCGACATCAACTGGGTC CGCCAGACCCCTGAGCAGGGCCTGGAATGGATGGCGGCATCTCCCTGGCGAC GGCAACACCAACTACAACGAGAACTTCAAGGGCAGAGTGACCATGACCAGGGACA CCTCTAACTCCACCGCTACATGGAACCTGCCGGCTGAGATCCGACGACACCGCC GTGTACTACTGGCCAGGACGGCAACTTCCCTTACTACGCCATGACTCTTGGGG CCAGGCCACACCGTGACAGTGTCTCTGGCGGAGGAAGTGGAGTGGAGG ATCTGGCGGAGGGCTCCGATGTGTGTCATGACCCAGTCCCACTGTCCCTGCCCT GTGACCCCTGGCGAGCCTGCCATCTCTGCGGCTCCCTCCAGTCCCTGTGTGT ACTCCAACGGCAATACCTACCTGACCTGGTATCAGCAGAAGCCTGGCCAGTCCCT AGGCTGCTGATCTACAAGGTGCCAACCGTTCTCCGGCTGCCCGACAGATTCTC CGGCTCGGGCTCTGGCACCGACTTCAACATGAAGATCTCCAGGGTGGAGGCTGAG GACGTGGGCGGTACTTCTGCTCCAGTCCACCCACGTGCCCTACACCTTCGGACA GGCACCAAGCTGGAATCAAGTCTGGCGGAGGGGCTCTGAAGTGCAGCTGGTG GAAAGCGGAGGGGACTGGTGAGCCCGGGGGAATTGGTCCGACAGGCCCCAG GCCAGCGGCTTACCTTCAACAAGTACGCCATGAATTGGTCCGACAGGCCCCAG GGAAGGCCTGGAATGGTGGCAGCGGATCCGGTCCAAGTACAACAACACGCCAC CTACTACGCTGACTCCGTGAAGGACAGATTACCATCAGCCGGGACGACTCTAAGA ACACCGCTATCTGCAGATGAACAACCTGAACAACCGAGGATACAGCTGTACTATT GTGTGCGGCACGGCAACTTCGGCAACTCCTACATCTCCTACTGGCCTATTGGGA CAGGGAACACTGGTCACCGTGTCTAGCGAGGTGGCGAAGTGGGGAGGCGGA TCTGGCGGTGGGATCCAGACCGTGGTCAACCCAGGAACCTTCCCTGACCGTCT CCCAGCGGCACCGTGACCGTGAACCTGTGGTCTCTACCGCGCTGTGACCTC CGGCAACTACCTAAGTGGTGCAGCAGAAACCCGACAGGCTCCTAGAGGCCTG ATCGCGGCACCAAGTTCTGGCCCTGGCAGCCCTGCCAGATTCTCCGGCTCCC TGCTGGAGGCAAGGCCGCTCTGACCCCTGTGGCGTGCAGCCTGAGGACGAGG CCGAGTACTACTGT AAAGCTGACCGTGTCTG</p>
869.	PM08B6-H	artificial	aa	<p>QVQLVQSGAEVMKPGASVKVSKASGYTITDYMWDWVRQAPGQGLEWIRIDPANGD SKYDPKFQGRVTMTADTSTNTVMELSSLRSEDIAVYYCARGGMIWYFDWVGQGT TVSS</p>
870.	PM08B6-HCDR1	artificial	aa	DTYMD
871.	PM08B6-HCDR2	artificial	aa	RIDPANGDSKYDPKFQG

872.	PM08B6-HCDR3	artificial	aa	GGMIWYFDV
873.	PM08B6-H	artificial	nt	CAGGTGCAGCTGGTCCAGTCTGGGGCAGAGGTTATGAACACAGGGCCCTCAGTCA AGGTGCTCTGCAAGCTTCTGGCTACACCATACAGACACCTATATGGACTGGGTG AGGCAGGCGCTGGACAGGCGCTGGAATGATTGCAAGATTGATCTCGGAATG GTGATAGTAATATGACCCGAAATCCAGGGCAGGGTCACTATGACAGCAGACACA TCCACCAACACAGTCTACATGGAGCTCAGCAGCCTGAGATCTGAGGACACTGCCGT CTATTATTGTCTAGAGGCGGATGATATGGTACTTCGATGTCTGGGGCCCAAGGA CCAGGTACCCGTCCTCTCA
874.	PM08B6-L	artificial	aa	EIVLTQSPATLAVSPGEKVTLSASSSSSISNYLHWYQQKPLPRLLIYRTSNLASGVP DRFSGSGSGTDFTLTISRLEPEDFATYYCQQGSSLPYTFGQGTKLEIK
875.	PM08B6-LCDR1	artificial	aa	SASSISSNYLH
876.	PM08B6-LCDR2	artificial	aa	RTSNLAS
877.	PM08B6-LCDR3	artificial	aa	QQGSSLPYT
878.	PM08B6-L	artificial	nt	GAGATCGTGCTCACCCAGTCTCCAGCCACCCTGGCTGTATCTCCCGGGAGAGG TCACTCTCTCTGCAGTGCCAGCTCAAGTATAAGTCCAATTACTTGCAATTGGTATC AGCAGAAGCCAGGATTGCCCTAGACTCTTGATTTATAGACATCCAATCTGGCTT CTGGAGTCCCAGATCGCTTCACTGAGTGGCTGGGACCCGATTCTCACTCTCACA ATTAGCAGGCTGGAGCCTGAAGATTTGCCACTTACTACTGCCAGCAGGGTAGTAG TTTACCGTACACGTTCCGACAGGGACCAAGCTTGAGATCAAA
879.	PM08B6-HL	artificial	aa	QVQLVQSGAEVMPGASVKVSKASGYTIDTYMDWVRQAPGQGLEWIRIDPANGD SKYDPKFQGRVTMTADTSTNTVYMELSSLRSEDAVYVCARGMIWYFDVWGQGT TVSSGGGGSGGGGGGSEIVLTQSPATLAVSPGEKVTLSASSSISNYLHWYQ QKPLPRLLIYRTSNLASGVPDRFSGSGSGTDFTLTISRLEPEDFATYYCQQGSSLPY TFGQGTKLEIK
880.	PM08B6-HL	artificial	nt	CAGGTGCAGCTGGTCCAGTCTGGGGCAGAGGTTATGAACACAGGGCCCTCAGTCA AGGTGCTCTGCAAGCTTCTGGCTACACCATACAGACACCTATATGGACTGGGTG AGGCAGGCGCTGGACAGGCGCTGGAATGATTGCAAGATTGATCTCGGAATG GTGATAGTAATATGACCCGAAATCCAGGGCAGGGTCACTATGACAGCAGACACA TCCACCAACACAGTCTACATGGAGCTCAGCAGCCTGAGATCTGAGGACACTGCCGT CTATTATTGTCTAGAGGCGGATGATATGGTACTTCGATGTCTGGGGCCCAAGGA CCAGGTACCCGTCCTCTCAGGTGGTGGTCTGCGGCGGCGCTCCGGTG GTGGTGGTCTGAGATCGTCTCACCCAGTCTCCAGCCACCCTGGCTGTATCTCC GGGAGAGAGGTCACTCTCTCTGAGTCCAGTCCAGTCAAGTAAAGTCCAATTACTT GCATTGGTATCAGCAGAAGCCAGGATTGCCCCCTAGACTCTTGATTTATAGGACATC CAATCTGGCTTCTGGAGTCCAGATCGCTTCAGTGGCAGTGGGTCTGGGACCGATT

881.	PM08B6 HL X I2C HL	artificial	aa	TCACTCTCACAATTAGCAGGCTGGAGCCTGAAAGATTTTGGCAGTTACTACTGCCAGC AGGGTAGTAGTTACCGTACACGTTCCGACAAAGGACCAAGCTTGAGATCAAA QVQLVQSGAEVMKPGASVKVSKASGYTIDTYMDWVRQAPGQGLEWRIADPANGD SKYDPKFQGRVTMTADSTNTVMELSSLRSEDVAVYCARGMWYFDWVGQGTTV TVSSGGGGGGGGGGSEIVLTQSPATLAVSPGEKVTLSGSSSSSYNYLHWYQ QKPLPPRLIYRTSNLASGVPDRFSGSGSTFTLTISRLEPEDFATYCCQGSLLPY TFGGGTLEIKSGGGSEVQLVESGGGLVQPGGSLKLSAASGFTFNKYAMNWVRQA PGKLEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNLLKTEDTAVYVC VRHGNFNSYISYWAYWGQGLTVTVSSGGGGGGGGGGGSGQTVVTQEPSLTVSP GGTVLTCGSSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTPARFSGSLLGG KAALTLSGVQPEDEAEYCYLVWYSNRWVFGGKLTVL CAGGTGCAGCTGGTCCAGTCTGGGGCAGAGGTATGAAACCAGGGGCTCAGTCA AGGTGCTCTGCAAAAGCTTCTGGCTACACCATACAGACACCTATATGACTGGGTG AGGCAGGGCGCTGGACAGGGCCTGGAATGGATTGCAAGGATTGATCCTGCCAATG GTGATAGTAAATATGACCCGAAATCCAGGGCAGGGTCACTATGACAGCAGACACA TCCACCAACACAGTCTACATGGAGCTCAGCAGCCTGAGATCTGAGGACACTGCCGT CTATTATTGTCTAGAGCGGGATGATGTTGTTCTGCTGCTGGGCGGCTCCGGTG CCAGGTCACCGTCTCCTCAGGTGGTGGTCTGCGGGCGGCTCCGGTG GTGGTGTCTGAGATCGTCTCAGCTCAGCCAGTCTCAGCCACCTGGCTGATCTCCC GGGAGAAGGTCACTCTCTCTGAGTGCCAGTCCAGCTCAAGTATAAGTCCAAATACCT GCATTGGTATCAGCAGAGCCAGGATTGCCCTAGACTCTTGATTTATAGGACATC CAATCTGGCTCTGGAGTCCCAGATCGCTTCAGTGGCAGTGGTCTGGGACCGATT TCACTCTCACAATTAGCAGGCTGGAGCCTGAAGATTTTGGCAGTTACTACTGCCAGC AGGGTAGTAGTTTACCGTACACGTTCCGACAAAGGACCAAGCTTGAGATCAAATCC GGAGGTGGTGGATCCGAGGTGCAGCTGGTCCGAGTCTGGAGGAGGATTGGTGCAG CCTGGAGGGTCAATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAATAAGTAC GCCATGAAGTGGTCCGCGAGGCTCCAGGAAAGGTTTGGAAATGGTGTCTCGCA TAAGAAGTAAATATAATTAATGCAACATATTATGCCGATTCAAGTGAAGACAGGTT CACCATCTCCAGAGATGATTCAAAACACACTGCCTATCTACAAATGAACACTTGAA AACTGAGGACACTGCCGTGACTACTGTGTGAGACATGGGAACCTCGGTAATAGCT ACATATCTACTGGGCTTACTGGGGCCAAAGGACTCTGGTCAACCTCTCCTCAGGT GGTGGTGGTCTGGCGGGCGGCTCCGGTGGTGGTCTCAGACTGTTGTGA CTCAGGAACCTTCACTCACCGTATCACCTGGTGGAAACAGTCACTCACTTGTGGC TCCTCGAGTGGGGCTGTTACATCTGGCAACTACCCAACTGGGTCCAAACAAACCC AGGTCAGGCACCCCGTGGTCTAATAGGTGGGACTAAGTTCTCGCCCCCGGTACT CCTGCCAGATTCTCAGGCTCCCTGCTTGGAGGCAAGGCTGCCCTCACCCCTCTCAG
882.	PM08B6 HL X I2C HL	artificial	nt	

55					GGGTACAGCCAGAGGATGAGGCAGAAATATTACTGTGTTCTATGGTACAGCAACCGC TGGGTGTTCCGGTGGAGGAACCAACTGACTGTCCTA
50	883.	PM08B6-H codon optimized	artificial	nt	CAGGTGCAGCTGGTCCAGTCTGGCGCCGAAGTGATGAAGCCTGGCGCCTCCGTGA AGGTGCTCTGCAAGGCCTCCGGCTACACCATCACCGACACCTACATGGACTGGGT GGGGAGGCTCCTGGACAGGGCCTGGAATGATGATGCCGGATCGACCTGCCAA CGCGGACTCCAAGTACGACCCCTAAGTTCAGGGCAGAGTACCATGACCCGCCGAC ACCTCCACCACACCGGTGTACATGGAACGTCTCCCTGCGGTCTGAGGACACCGC CGTGTACTACTGCGCCAGGGCGGCATGATCTGGTACTTCGACGTGTGGGGCCAG GGCACCACCGTGACAGTGTCTCT
45	884.	PM08B6-L codon optimized	artificial	nt	GAGATCGTGTGACCCAGTCTCTCCACCCCTGGCTGTGTCTCCCGCGGAGAAAG TGACCTGTCTGTCTCGCTCCGCTCTCTCCATCTCCTCAACTACCTGCACCTGGTATC AGCAGAAACCTGGCTGCTCTCGCTCTCGGTCTGATCTACCGACCTCCAACCTGGC CTCTGGCGTGGCGGACAGGTCTCTCGGTCTGGCTCGGCACCGACTTCACCTG ACCATCTCCGGGTGAACTGAGGACTTCGCCACCTACTACTGCCAGCAGGGCT CCTCCTGCCTTACACCTTCGGACAGGGCACCAAGCTGGAATCAAG
40	885.	PM08B6-HL codon optimized	artificial	nt	CAGGTGCAGCTGGTCCAGTCTGGCGCCGAAGTGATGAAGCCTGGCGCCTCCGTGA AGGTGCTCTGCAAGGCCTCCGGCTACACCATCACCGACACCTACATGGACTGGT GGGGAGGCTCCTGGACAGGGCCTGGAATGATGATGCCGGATCGACCTGCCAA CGCGGACTCCAAGTACGACCCCTAAGTTCAGGGCAGAGTACCATGACCCGCCGAC ACCTCCACCACACCGGTGTACATGGAACGTCTCCCTGCGGTCTGGCTGCTATACCG CGTGTACTACTGCGCCAGGGCGGCATGATCTGGTACTTCGACGTGTGGGGCCAG GGCACCACCGTGACAGTGTCTCTGGCGCCGAAGTGATGATCTCGACGTGTGGGCCAG GGCACCACCGTGACAGTGTCTCTGGCGCCGAAGTGAGGTGGAGGATCT GGTGGAGCGGCTCCGAGATCGTGTGACCCAGTCTCTGCCACCTGGCTGTGT CTCCGGCGAGAAAGTACCCCTGTCTGCTCGGCTCTCTCCATCTCTCCAAAC TACCTGCACTGGTATCAGCAGAAACCTGGCTGCTCTCGGTCTGCTGATCTACCG GACCTCCAAACCTGGCTCTGGCTGCGCGCCGACAGGTTCTCCGGCTCTGGCTCCGGC ACCGACTTCACCTGACCATCTCCGGCTGGAACCTGAGGACTTCGCCACCTACTA CTGCCAGCAGGGCTCCTCCTCGCTTACACCTTCGGACAGGGCACCAAGCTGGAA ATCAAG
35	886.	PM08B6 HL x I2C HL codon optimized	artificial	nt	CAGGTGCAGCTGGTCCAGTCTGGCGCCGAAGTGATGAAGCCTGGCGCCTCCGTGA AGGTGCTCTGCAAGGCCTCCGGCTACACCATCACCGACACCTACATGGACTGGT GGGGAGGCTCCTGGACAGGGCCTGGAATGATGATGCCGGATCGACCTGCCAA CGCGGACTCCAAGTACGACCCCTAAGTTCAGGGCAGAGTACCATGACCCGCCGAC ACCTCCACCACACCGGTGTACATGGAACGTCTCCCTGCGGTCTGAGGACACCGC CGTGTACTACTGCGCCAGGGCGGCATGATCTGGTACTTCGACGTGTGGGGCCAG GGCACCACCGTGACAGTGTCTCTGGCGCCGAAGTGAGGTGGAGGATCT

				GGTGGAGGGGCTCCGAGATCGTGTGACCCAGTCTCCTGCCACCCCTGGCTGTGT CTCCGGCGAGAAAGTGACCCCTGTCTCTCGCCCTCCTCCTCATCTCCTCCAAAC TACCTGCACTGGTATCAGCAGAAAGCCTGGCTGCCCTCCTCGGCTGCTGATCTACCG GACCTCCAACCTGGCTCTGGCGTGCCGACAGGTTCTCCGGCTCTGGCTCCGGC ACCGACTTCACCCTGACCATCTCCGGCTGGAACCTGAGGACTTCGCCACCTACTA CTGCCAGCAGGGCTCCTCCCTGCCTTACACCTTCGGACAGGGACCAAGCTGGAA ATCAAGTCTGGCGGAGGGGCTCTGAAGTGCAGCTGGTGAAGCGGAGGGGGA CTGGTGACGCCCCGGGGAAGTCTGAAGCTGTCTGTGCCCGCAGCGCTTTACCT TCAACAAGTACGCCATGAATTGGTCCGACAGGCCCCAGGGAAGGCTTGAATG GGTGACGCGATCCGGTCCAAGTACAACAACCTACGCCACCTACTACGCTGACTCCG TGAAGGACAGATTCAACATCAGCCGGGACGACTCTAAGAACACCCCTATCTGCAG ATGAACAACCTGAAACCCGAGGATACAGCTGTGTACTATTGTGTGCGGCACGGCAA CTTCGGCAACTCTACATCTCCTACTGGGCTATTGGGACAGGGAACACTGGTCA CCGTGTCTAGCGGAGGTGGCGAAGTGGGAGGCGGATCTGCGGTGGCGGAT CCAGACCGTGGTCAACCAGGAACCTTCCCTGACCGCTCTCCCAAGCGGCACCGT GACCTGACCTGTGGTCTCTACCGGCGCTGTGACCTCCGGCAACTACCTAACT GGTGACAGAAACCCGACAGGCTCTTAGAGGCTGATCGGCGGACCAAGTT TCTGGCCCTGGACCCCTGCCAGATTCTCCGGTCCCTGCTGGAGGCAAGGCC GCTCTGACCCCTGTCTGGCGTGACGCTGAGGACGAGGCGGAGTACTACTGTGTC TGTGTACTCCCAACAGATGGGTGTTCCGAGGCGGCACAAAGCTGACCGTGTCTG
887.	PM08E11-H	artificial	aa	QQLVQSGAEVMKPGASVKVSKASGYTITDYMWDVVRQAPGQGLEWIARIDPANGD SKYDPKFQGRVTMTADTSTNTVYMESSLRSEDTAVYYCARGGMWYFDVWGQGTIV TVSS
888.	PM08E11-HCDR1	artificial	aa	DTYMD
889.	PM08E11-HCDR2	artificial	aa	RIDPANGDSKYDPKFQG
890.	PM08E11-HCDR3	artificial	aa	GGMIWYFDV
891.	PM08E11-H	artificial	nt	CAGGTGCAGCTGGTCCAGTCTGGGCGCAGAGGTTATGAAACCCAGGGGCTCAGTCA AGGTGTCCTGCAAGCTTCTGGCTACACCATACAGACACCTATATGGACTGGGTG AGCAGGCGCCTGGACAGGGCCTGGAATGGATTGCAAGGATTGATCCTGCCAATG GTGATAGTAAATATGACCCGAAATCCAGGGCAGGGTCACTATGACAGCAGACACA TCCACCAACACAGTCTACATGGAGCTCAGCAGCCTGAGATCTGAGGACACTGCCGT CTATTATTGTCTAGAGCGGGATGATATGGTACTTCGATGCTGGGGCCAAGGGA CCACGGTCCCGTCTCCTCA
892.	PM08E11-L	artificial	aa	EIVLTQSPATMSVSPGERATLSCSASSSSISNYLHWYQQKPLPRLIYRTSNLASGIP DRFSGSGSGTDFTLTISRLEAEDFATYCCQQGSSLPYTFGQGTKLEIK
893.	PM08E11-LCDR1	artificial	aa	SASSSSISNYLH

894.	PM08E11-LCDR2	artificial	aa	RTSNLAS	
895.	PM08E11-LCDR3	artificial	aa	QQGSSSLPYT	
896.	PM08E11-L	artificial	nt	GAGATCGTGTGCTCACCCAGTCTCCAGCCACCATTGCTGTATCTCCCGGGGAGAGGG CCACTCTCTCTGAGTCCAGTCCAGTCAAGTATAAGTTCCAAATTGCTGCAATGCTGATC AGCAGAAGCCAGGATTGCCCCCTAGACTCTTGATTTATAGGACATCCAACTGCGCTT CTGGAATCCAGATCGCTTCACTGCGAGTGGTCTGGGACCGATTTCACTCTCACA ATTAGCAGGCTGGAGGCTGAAGATTTTCCCACTTACTACTGCCAGCAGGCTAGTAG TTTACCGTACACGTTCCGACCAAGGACCAAGCTTGAGATCAAA	
897.	PM08E11-HL	artificial	aa	QVQLVQSGAEVMKPGASVKVCKASGYTITDYMWVRQAPGQGLEWIRIDPANGD SKYDPKFQGRVTMTADTSTNTVMELSSLRSEDAVYYCARGGMIWYFDVWGQGTTV TVSSGGGGSGGGGGGSEIVLTQSPATMSVSPGERATLSCSASSISSNYLHWYQ QKPLPRLLIYRTSNLASGIPDRFSGSGSGTDFTLTISRLEAEDFATYYCQQGSSSLPYT FGQGTKLEIK	
898.	PM08E11-HL	artificial	nt	CAGGTGCAGCTGGTCCAGTCTGGGGCAGAGGTTATGAAACCAGGGGCGCTCAGTCA AGGTGCTCTGCAAGCTTCTGGCTACACCATACAGACACCTATATGGACTGGTG AGGCAGGCGCTGGACAGGGCCTGGAATGGATTGCAAGGATTGATCCTGCGAATG GTGATAGTAAATATGACCCGAAATCCAGGGCAGGTCACATGACAGCAGACACA TCCACCAACACAGTCTACATGGAGCTCAGCAGCTGAGATCTGAGGACACTGCCGT CTATTATTGTCTAGAGCGGGGATGATATGGTACTTCTGGCGGCGGCTCCGGT CCAGGTCACCGTCTCCTCAGGTGGTGGTGGTCTGGCGGCGGCTCCGGT GTGGTGTCTGAGATCGTGTCAACCCAGTCTCCAGCCACCATGCTGTATCTCCC GGGAGAGGGCCACTCTCCTGCAGTCCAGTCCAGCTCAAGTATAAGTTCCAATTACTT GCATTGGTATCAGCAGAAGCCAGGATTGCCCCCTAGACTCTTGATTTATAGGACATC CAATCTGGCTTCTGGAATCCAGATCGCTTCAGTGGCAGTGGTCTGGGACCGATT TCACTCTCACAAATTAGCAGGCTGGAGGCTGAAGATTTTGCACATTACTACTGCCAGC AGGTTAGTAGTTTACCGTACACGTTCCGACCAAGGACCAAGCTTGAGATCAAA	
899.	PM08E11 HL X I2C HL	artificial	aa	QVQLVQSGAEVMKPGASVKVCKASGYTITDYMWVRQAPGQGLEWIRIDPANGD SKYDPKFQGRVTMTADTSTNTVMELSSLRSEDAVYYCARGGMIWYFDVWGQGTTV TVSSGGGGSGGGGGGSEIVLTQSPATMSVSPGERATLSCSASSISSNYLHWYQ QKPLPRLLIYRTSNLASGIPDRFSGSGSGTDFTLTISRLEAEDFATYYCQQGSSSLPYT FGQGTKLEIKSGGGGSEVQLVESGGGLVQPGSLKLSAASGFTFNKYAMNWRQAP GKLEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCV RHGNFGNSYISYWAYWGQGLTVTVSSGGGGSGGGGGSGTQVTVQEPSLTVSPG GTVTLTCSGSTGAVTSGNYPNWWQKPGQAPRGIGTKFLAPGTPTARFSGSLLGK AALTLSGVQPEDEAEYYCVLWYSNRWVFGGGLTVL	
900.	PM08E11 HL X I2C	artificial	nt	CAGGTGCAGCTGGTCCAGTCTGGGGCAGAGGTTATGAAACCAGGGGCGCTCAGTCA	

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55	903.		PM08E11-HL codon optimized	artificial	nt	<p> CCTCTGGCATCCCGGACAGGTTCTCCGGCTCTGGCTCCGGACCGGACTTCACCCCT GACCATCTCCCGGCTGGAAGCTGAGGACTTCGCCACCTACTACTGCCAGCAGGGC TCCTCCCTGCCTTACACCTTCGGACAGGGCACCAAGCTGGAATCAAG CAGGTGCAGCTGGTCCAGTCTGGCGCCGAAGTGATGAAGCCTGGCGCCTCCGTGA AGGTGTCTCTGAAGGCTCCGGCTACACCATACCGACACCTACATGAGACTGGGT GGCGCAGGCTCCTGGACAGGGCCTGGAATGGATGATCGCCCGGATCGACCTGCCAA CGCGACTCCAAGTACGACCCCTAAGTTCAGGGCAGAGTGACCATGACCGCCGAC ACCTCCACCAACACCGGTGTACATGGAATGTCTCCCTGCGGTCTGAGGACACCGC CGTGTACTACTGCGCCAGGGCGGCATGATCTGGTACTTCGACGTGTGGGGCCAG GGCACCCGTGACAGTGTCTCTGGCGCGGAGGAAGTGAGGTGGAGGATCT GGTGGAGGGCTCCGAGATCGTGTGACCCAGTCTCCTGCCACCATGTCTGTGT CTCCCGCGGAGAGCCACCTGTCTGCTCCGCTCCTCCTCCATCTCCTCCAA TACCTGCACTGGTATCAGCAGAAGCCTGGCTGCTCCCTGCTGCTGCTGCTACCG GACCTCCAACCTGGCTGTGCTATCCCGGCTGGAAGTCTCCGGCTCTGGCTCCGGC ACCGACTTCAACCTGACCATCTCCGGCTGGAAGTCTGAGGACTTCGCCACCTACTA CTGCCAGCAGGGCTCCTCCCTGCTTACACCTTCGGACAGGGCACCAAGCTGGAA ATCAAG </p>
50						
45						
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	904.		PM08E11 HL x 12C HL codon optimized	artificial	nt	<p> CAGGTGCAGCTGGTCCAGTCTGGCGCCGAAGTGATGAAGCCTGGCGCCTCCGTGA AGGTGTCTCTGAAGGCTCCGGCTACACCATACCGACACCTACATGAGACTGGGT GGCGCAGGCTCCTGGACAGGGCCTGGAATGGATGATCGCCCGGATCGACCTGCCAA CGCGACTCCAAGTACGACCCCTAAGTTCAGGGCAGAGTGACCATGACCGCCGAC ACCTCCACCAACACCGGTGTACATGGAATGTCTCCCTGCGGTCTGAGGACACCGC CGTGTACTACTGCGCCAGGGCGGCATGATCTGGTACTTCGACGTGTGGGGCCAG GGCACCCGTGACAGTGTCTCTGGCGCGGAGGAAGTGAGGTGGAGGATCT GGTGGAGGGCTCCGAGATCGTGTGACCCAGTCTCCTGCCACCATGTCTGTGT CTCCCGCGGAGAGCCACCTGTCTGCTCCGCTCCTCCTCCATCTCCTCCAA TACCTGCACTGGTATCAGCAGAAGCCTGGCTGCTCCCTCCTGCTGCTGCTACCG GACCTCCAACCTGGCTCTGGATCCCGACAGGTTCTCCGGCTCTGGCTCCGGC ACCGACTTCAACCTGACCATCTCCCGGCTGGAAGTCTGAGGACTTCGCCACCTACTA CTGCCAGCAGGGCTCCTCCCTGCTTACACCTTCGACAGGGCACCAAGCTGGAA ATCAAGTCTGGCGGAGGGGCTCTGAAGTGCAGCTGGTGAAGCGGAGGGGA CTGGTGCAGCCCGGGGAAGTCTGAAGTGTCTGTGCGCGCAGGGCTTTACCT TCAACAAGTACGCCATGAATTGGTCCGACAGGCCCGACCGAAAGCCTTGAATG GGTGGCACGGATCCGGTCCAAGTACAACACTACGCCACCTACTACGCTGACTCCG TGAAGGACAGATTCAACCATCAGCGGGGACGACTCTAAGAACACCGCCTATCTGACG ATGAACAACCTGAAACCGAGGATACAGCTGTGTACTATTGTGCGGCACGGCAA </p>

				CTTCGGCAACTCCTACATCCTCTACTGGCCCTATTGGGGACAGGGAACACTGGTCA CCGTGTCTAGCGGAGGTGGCGAAGTGGGGAGGCGGATCTGGCGTGGCGGAT CCAGACCGTGGTACCCAGGAACCTTCCCTGACCGTCTCCCAAGCGGACCCGT GACCTGACCTGTGGCTCCTCTACGGCGCTGTGACCTCCGGCAACTACCCCTAACT GGGTGCAGCAGAAACCCGACAGGCTCTAGAGCCCTGATCGGCGCACCAAGTT TCTGGCCCTGGCACCCCTGCCAGATTCTCCGGCTCCCTGCTGGAGGCAAGGCC GCTCTGACCCCTGTGGCGTGCAGCCTGAGGACGAGGCCGAGTACTACTGTGTGC TGTGTACTCCAACAGATGGGTGTTGGAGGCGGCACAAAGCTGACCGTGTCTG
905.	PM95H6-H	artificial	aa	QVQLVQSGAEVMKPGASVKVSKASGYNFKDTYMDWVKQTPEQGLEWMGRIDPANG DSKYDPKFQGRVTITADTSTNTAYMELSSLRSEDTAVYVCARGGMIWYFDVWGQGTTV TVSS
906.	PM95H6-HCDR1	artificial	aa	DTYMD
907.	PM95H6-HCDR2	artificial	aa	RIDPANGDSKYDPKFQG
908.	PM95H6-HCDR3	artificial	aa	GGMIWYFDV
909.	PM95H6-H	artificial	nt	CAGGTGCAGCTGGTCCAGTCTGGGGCAGAGGTTATGAAGCCAGGGGCCCTCAGTCA AGGTGTCCTGCAAGCTTCTGGCTACAACTTTAAAGACACCTATATGGACTGGGTGA AGCAGACGCCCTGAACAGGGCTGGAATGATGGAAGGATTGATCCTCGGAATGG TGATAGTAATATGACCCGAAATTCAGGCGAGGTCACATAACAGCAGACACAT CCACCAACACAGCCTACATGGAGCTCAGCAGCCTGAGATCTGAGGACACTGCCGT CTATTATTGTGCTAGAGGCGGATGATATGTTGCTCGATGCTGGGGCCAAAGGGA CCAGGTCACCGTCTCCTCA
910.	PM95H6-L	artificial	aa	EIVLTQSPATLAVSPGKVTLSASSSSISNYLHWYQQKPKLPRLIYRTSNLASGVP DRFSGSGSGTDFTLTISRLEPEDFATYVCQQGSSLPYTFGQGTKEIK
911.	PM95H6-LCDR1	artificial	aa	SASSSSISNYLH
912.	PM95H6-LCDR2	artificial	aa	RTSNLAS
913.	PM95H6-LCDR3	artificial	aa	QQGSSLPYT
914.	PM95H6-L	artificial	nt	GAGATCGTGTCTCACCCAGTCTCCAGCCACCCTGGCTGTATCTCCCGGGAGAAGG TCACTCTCTCTGCAGTGCCAGCTCAAGTATAAGTCCAATTACTTGCAATTGATC AGCAGAAGCCAGATTGCCCTAGACTCTTGATTTATAGACATCCAATCTGGCTT CTGGAGTCCCAGATCGCTTCAGTGGCAGTGGGTCTGGACCCGATTTCACCTCACA ATTAGCAGGCTGGAGCCTGAAGATTTTGGCACTTACTACTGCCAGCAGGCTAGTAG TTTACCGTACACGTTCCGACAAGGACCAAGCTTGAGATCAA
915.	PM95H6-HL	artificial	aa	QVQLVQSGAEVMKPGASVKVSKASGYNFKDTYMDWVKQTPEQGLEWMGRIDPANG DSKYDPKFQGRVTITADTSTNTAYMELSSLRSEDTAVYVCARGGMIWYFDVWGQGTTV TVSSGGGSGGGGGGGGSEIVLTQSPATLAVSPGKVTLSASSSSISNYLHWYQ QKPLPRLIYRTSNLASGVPDRFSGSGSGTDFTLTISRLEPEDFATYVCQQGSSLPY

55	916.	PM95H6-HL	artificial	nt	TFGQGTKEIK CAGGTGCAGCTGGTCCAGTCTGGGGCAGAGGTTATGAAGCCAGGGGCTCAGTCA AGGTGCTCTGCAAGCTTCTGGCTACAACCTTTAAAGACACCTATATGGACTGGTGA AGCAGACGCTGAACAGGGCTGGAATGGATGGAGGATTGATCTGCGAATGG TGATAGTAAATATGACCCGAAATTCAGGGCAGGTCACATATAACAGCAGACACAT CCACCAACACAGCCTACATGGAGCTCAGCAGCCTGAGATCTGAGGACACTGCCGT CTATTATTGTCTAGAGCGGGATGATATGGTACTTCGATCTGGGGCCAAAGGA CCACGGTACCGTCTCTCAGGTGGTGGTCTGGGGCGGGCTCCGGTG GTGGTGTCTGAGATCGTCTCACCCAGTCTCCAGCCACCTGGCTGTATCTCCC GGGAGAAGGTCACTCTCTCTGAGTCCAGTCCAGCTCAAGTATAAGTCCAAATTACTT GCATTGGTATCAGCAGAAGCCAGGATTGCCCCCTAGACTCTTGATTTATAGGACATC CAATCTGGCTTCTGGAGTCCAGATCGCTTCAGTGGCAGTGGTCTGGAGCCGATT TCACTCTCACAATTAGCAGGCTGGAGCCTGAAGATTTGCCACTTACTACTGCCAGC AGGTAGTAGTTTACCGTACACGTTCCGACAAGGACCAAGCTTGAGATCAAA QVQLVQSGAEVMPGASVKVSKASGYNFKDITYMDWVKQTPQQGLEWMGRIDPANG DSKYDPKFQGRVTITADTSTNTAYMELSSLRSEDTAVYYCARGGMWYFDVWGQGTIV TVSSGGGSGGGSGGGSEIVLTQSPATLAVSPGEKVTLSASSSSISNLYLHWYQ QKPLPRLLIYRTSNLASGVPDFRFGSGSGDTFTLTISRLEPEDFATYYCQGGSSLPY TFGQGTKEIKSGGGSEVQLVESGGGLVQPGSLKLSAASGFTFNKYAMNWVRQA PGKLEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNLLKTEDTAVYYC VRHGNFGNSYISYWAYWGQGLVTVSSGGGSGGGSGGGGSGQTVVTQEPSLTVSP GGTVTLTCGSSSTGAVTSGNYPNWVQQKPGQAPRGLIGTKFLAPGTPARFSGSLLGG KAALTLGVQPEDEAEYYCVLWYSNRWVFGGKLTVL
50	917.	PM95H6 HL X I2C HL	artificial	aa	QVQLVQSGAEVMPGASVKVSKASGYNFKDITYMDWVKQTPQQGLEWMGRIDPANG DSKYDPKFQGRVTITADTSTNTAYMELSSLRSEDTAVYYCARGGMWYFDVWGQGTIV TVSSGGGSGGGSGGGSEIVLTQSPATLAVSPGEKVTLSASSSSISNLYLHWYQ QKPLPRLLIYRTSNLASGVPDFRFGSGSGDTFTLTISRLEPEDFATYYCQGGSSLPY TFGQGTKEIKSGGGSEVQLVESGGGLVQPGSLKLSAASGFTFNKYAMNWVRQA PGKLEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNLLKTEDTAVYYC VRHGNFGNSYISYWAYWGQGLVTVSSGGGSGGGSGGGGSGQTVVTQEPSLTVSP GGTVTLTCGSSSTGAVTSGNYPNWVQQKPGQAPRGLIGTKFLAPGTPARFSGSLLGG KAALTLGVQPEDEAEYYCVLWYSNRWVFGGKLTVL
5	918.	PM95H6 HL X I2C HL	artificial	nt	CAGGTGCAGCTGGTCCAGTCTGGGGCAGAGGTTATGAAGCCAGGGGCTCAGTCA AGGTGCTCTGCAAGCTTCTGGCTACAACCTTTAAAGACACCTATATGGACTGGTGA AGCAGACGCTGAACAGGGCTGGAATGGATGGAGGATTGATCTGCGAATGG TGATAGTAAATATGACCCGAAATTCAGGGCAGGTCACATATAACAGCAGACACAT CCACCAACACAGCCTACATGGAGCTCAGCAGCCTGAGATCTGAGGACACTGCCGT CTATTATTGTCTAGAGCGGGATGATATGGTACTTCGATCTGGGGCCAAAGGA CCACGGTACCGTCTCTCAGGTGGTGGTCTGGGGCGGGCTCCGGTG GTGGTGTCTGAGATCGTCTCACCCAGTCTCCAGCCACCTGGCTGTATCTCCC GGGAGAAGGTCACTCTCTCTCAGTCCAGTCCAGCTCAAGTATAAGTCCAAATTACTT GCATTGGTATCAGCAGAAGCCAGGATTGCCCCCTAGACTCTTGATTTATAGGACATC CAATCTGGCTTCTGGAGTCCAGATCGCTTCAGTGGCAGTGGGCTGGGACCCGATT TCACTCTCACAATTAGCAGGCTGGAGCCTGAAGATTTGCCACTTACTACTGCCAGC AGGTAGTAGTTTACCGTACACGTTCCGACAAGGGGACCAAGCTTGAGATCAAAATCC

55	919.	PM95H6-H codon optimized	artificial	nt	GGAGGTGGTGATCCGAGGTGCAGCTGGTGGAGTCTGGAGGAGGATTGGTGCAG CCTGGAGGGTCAATTGAAACTCTCATGTGCAGCCTCTGGATTCACTTCAATAAGTAC GCCATGAAGTGGTCCGCCAGGCTCCAGGAAAGGTTTGAATGGTGGTTCGTCGCA TAAGAAGTAAATATAATATGCAACATATTATGCCGATGAGTGAAGACAGGTT CACCATCTCCAGAGATGATCAAAAACACTGCCTATCTACAAATGAACAATTGAA AACTGAGGACACTGCCGTGTAAGTGTGAGACATGGAACTTCGGTAATAGCT ACATATCCTACTGGGCTTACTGGGCCAAGGACTCTGTACCCCTCCTCAGGT GGTGGTGGTCTGGCGCGCGGCTCCGGTGGTGGTCTCAGACTGTTGTGA CTCAGGAACCTTCACTACCGTATCACCTGGTGAACAGTCACTCACTTGTGGC TCCTCGACTGGGCTGTTACATCTGGCAACTACCCAACTGGTCCAAACAAACC AGGTACGGCACCCCGTGGTCTAATAGGTGGACTAAGTTCCTCGCCCCGGTACT CCTGCCAGATTCTCAGGCTCCCTGCTTGGAGGCAAGGTGCCCTCACCCCTCTCAG GGGTACAGCCAGAGGATGAGGCAGAAATATTACTGTCTATGGTACAGCAACCGC TGGGTGTTCCGGTGAGGAACCAACTGACTGTCCTA
50	920.	PM95H6-L codon optimized	artificial	nt	CAGGTGCAGCTGGTCCAGTCTGGCGCCGAAGTGATGAAGCCTGGCGCCTCCGTGA AGGTGTCCTGCAAGGCCCTCCGGCTACAACCTCAAGGACACCTACATGGACTGGGTG AAACAGACCCCTGAGCAGGCGCTGGAATGGATGGCCGGATGACCCCTGCCAACG GCAGTCCAAGTACGACCCCTAAGTTCAGGGCAGAGTACCATCACCGCCGACAC CTCACCAACACCGCCTACATGGAACGTCTCCCTCGGTCTGAGGACACCGCC GTGTAATACTGCGCCAGGGCGGCATGATCTGGTACTTCGACGCTGGGGCCAGG GCACCCCGTGACAGTGTCTCT
45	921.	PM95H6-HL codon optimized	artificial	nt	GAGATCGTGTGACCCAGTCTCTGCCACCCCTGGCTGTGTCTCCCGGCGAGAAAG TGACCCCTGTCTGCTCCGCTCCTCCTCCATCTCCTCAACTACCTGCACTGGTATC AGCAGAAGCCTGGCCTGCCCTCCTCGGCTGTGATCTACCGACCTCCAACCTGGC CTCTGGCGTGCCCGACAGGTTCTCCGCTCTGGCTCCGGCACCGACTTCACCCCTG ACCATCTCCGGCTGGAACCTGAGGACTTCGCCACCTACTACTGCCAGCAGGGCT CCTCCCTGCCTTACACCTTCGGACAGGGCAACCAAGCTGGAATCAAG CAGGTGCAGCTGGTCCAGTCTGGCGCCGAAGTGATGAAGCCTGGCGCCTCCGTGA AGGTGTCCTGCAAGGCCCTCCGGCTACAACCTCAAGGACACCTACATGGACTGGGTG AAACAGACCCCTGAGCAGGCGCTGGAATGGATGGCCGGATCGACCCCTGCCAACG GCAGTCCAAGTACGACCCCTAAGTTCAGGGCAGAGTACCATCACCGCCGACAC CTCACCAACACCGCCTACATGGAACGTCTCCCTCGGTCTGAGGACACCGCC GTGTAATACTGCGCCAGGGCGGCATGATCTGGTACTTCGACGCTGGGGCCAGG GCACCCCGTGACAGTGTCTCTGGCGGCGGAGGAGTGAGGAGTGAGGATCTG GTGAGGCGGCTCCGAGATGTGCTGACCCAGTCTCTGCCACCTCCTGCTCCCTCAACT TCCCGGCGAGAAAGTGACCCCTGTCTGCTCCGCTCCTCCTCCTCCTCCTCAACT

55	922.	PM95H6 HL x I2C HL codon optimized	artificial	nt	ACCTGCACTGGTATCAGCAGAAAGCCTGGCCTGCCTCCTCGGCTGCTGATCTACCG GACCTCCAAACCTGGCCTCTGGCGTGCCGACAGGTTCTCCGCTCTGGCTCCGGC ACCGACTTCACTTACCATCTCCCGGCTGGAACCTGAGGACTTCCGACCTACTA CTGCCAGCAGGGCTCCTCCCTGCCTTACACCTTCGACACAGGCGCACCAAGCTGGAA ATCAAG CAGGTGCAGCTGGTCCAGTCTGGCGCCGAAAGTGATGAAGCCTGGCGCCTCCGTGA AGGTGCTCTGCAAGGCTCCGGCTACAACTTCAAGGACACCTACATGGACTGGTG AAACAGACCCCTGAGCAGGCTGGAATGGATGGCGGATCGACCCCTGCCAACG GCGACTCAAAGTACGACCCCTAAGTCCAGGGCAGAGTGACCATCACCGCCGACAC CTCACCAACACCCCTACATGAACTGTCTCCCTGCGTCTGAGGACACCGCC GTGTACTACTGCGCAGGGCGGCATGATCTGGTACTTCGACGTGTGGGCCAGG GCACCACTGTACAGTGTCTCTGGCGGCGGAGGAAGTGAGGTGGAGGATCTG GTGAGGCGGCTCCGAGATCGTCTGACCCAGTCTCTGCCACCTGGCTGTCTC TCCGGCGAGAAAGTGACCTGTCTGCTCCGCTCCTCCCTCCATCTCCTCCAAC ACCTGCACTGGTATCAGCAGAAAGCCTGGCCTGCCTCCTCGGCTGCTGATCTACCG GACCTCCAAACCTGGCCTCTGGCGTGCCGACAGGTTCTCCGCTCTGGCTCCGGC ACCGACTTCACTTACCATCTCCCGCTGGAACCTGAGGACTTCCGACCTACTA CTGCCAGCAGGGCTCCTCCCTGCCTTACACCTTCGACACAGGCGCACCAAGCTGGAA ATCAAGTCTGGCGAGGGGCTCTGAAGTGCAGTGTCTGCGGCGGCTTTACCT CTGGTGCAGCCCGGGGAGTCTGAAGTGTCTGCTGCGGCGGCTTTACCT TCAACAAGTACGCTATGAATTGGTCCGACAGGCGCCAGGAAAGGCTGGAATG GGTGGCAGGATCCGTCCTCAAGTACAACTACGCTACCTACTAGCTGACTCCG TGAAGGACAGATTACCATCAGCGGGACGACTCTAAGAACACCGCCTATCTGCAG ATGAACAACCTGAAACCGAGGATACAGCTGTGTACTATTGTGCGGCGACGGCAA CTTCCGCAACTCCTACATCTCTACTGGCCTATTGGGACAGGGAACACTGGTCA CCGTGTCTAGCGGAGGTGGCGGAAGTGGGGAGGCGGATCTGGCGGTGGCGGAT CCCAGACCGTGGTCAACCGAGAACCTTCCCTGACCGTCTCCCGAGGCGCACCGT GACCTGACCTGTGGCTCCTTACCGGCGCTGTGACCTCCGCAACTACCTTAAC GGTGCAGCAGAAACCGGACAGGCTCTAGAGGCTGTGCGGCGGACCAAGTT TCTGGCCCTGGCACCCCTGCCAGATTCTCCGCTCCTGCTGGAGGCGCAAGGCC GCTGTACCCCTGTCTGCGTGCAGCCTGAGGACGAGCGGCGGACTACTGTGTGC TGTGTACTCCAACAGATGGTGTTCGAGGCGGCGCACAAAGCTGACCGTGTCTG
50	923.	PM95A8-H	artificial	aa	QVQLVQSGAEVMKPGASVKVSKASGYNFKDTYMDWVKQTPEQGLEWMGRIDPANG DSKYDPKFQGRVTITADTSTNTAYMELSSLRSEDIAVYYCARGMIIWYFDVWGQGTIV TVSS
45	924.	PM95A8-HCDR1	artificial	aa	DTYMD

5
10
15
20
25
30
35
40
45
50
55

5
10
15
20
25
30
35
40
45
50
55

55	937.	PM95A8-H codon optimized	artificial	nt	GGGTACAGCCAGAGGATGAGGCAGAATATTACTGTGTTCTATGGTACAGCAACCGC TGGGTGTTCCGGTGGAGGAACCAAACTGACTGTCTTA CAGGTGCAGCTGGTCCAGTCTGGCGCCGAAGTGATGAAGCCTGGCGCCTCCGTGA AGGTGTCCTGCAAGGCCTCCGGCTACAACTTCAAGGACACCTACATGGACTGGGTG AAACAGACCCCTGAGCAGGGCCTGAATGGATGGCGGATCGACCTGCCAACG GCGACTCCAAGTACGACCCTAAGTTCAGGGCAGAGTGACCATCACCGCCGACAC CTCCACCAACACCGCCTACATGGAAGTGTCTCCCTCGGTCTGAGGACACCGCC GTGTACTACTGCGCCAGGGCGGCATGATCTGTGACTTCGACGTGTGGGCCAGG GCACCAACGTGACAGTGTCTCT
50	938.	PM95A8-HCDR1 codon optimized	artificial	nt	GAGATCGTGTGACCCAGTCTCTGCCACCATGTCCGTGTCTCCCGCGGAGAGGG CTACCCGTCTCTGCTCCGCCTCTCTCCATCTCTCCAACTACCTGCACCTGGTATC AGCAGAAGCCTGGCCTGCCCTCTCTCGGTCTGTATCTACCGGACCTCCAACCTGGC CTCTGGCATCCCCGACAGGTTCTCCGGCTCTGGTCCGGCACCGACTTCACCCCTG ACCATCTCCCGCTGGAAGCTGAGGACTTCGCCACCTACTACTGCCAGCAGGGCT CCTCCCTGCCCTTACACCTTCGGACAGGGCACCAAGCTGGAATCAAG CAGGTGCAGCTGGTCCAGTCTGGCGCCGAAGTGATGAAGCCTGGCGCCTCCGTGA AGGTGTCCTGCAAGGCCTCCGGCTACAACTTCAAGGACACCTACATGGACTGGTG AAACAGACCCCTGAGCAGGGCCTGGAATGGATGGCGGATCGACCTGCCAACG GCGACTCCAAGTACGACCCTAAGTTCAGGGCAGAGTGACCATCACCGCCGACAC CTCCACCAACACCGCCTACATGGAAGTGTCTCCCTCGGTCTGAGGACACCGCC GTGTACTACTGCGCCAGGGCGGCATGATCTGTGACTTCGACGTGTGGGCCAGG ATCAAG
45	939.	PM95A8-HCDR2 codon optimized	artificial	nt	GAGTGCAGCTGGTCCAGTCTGGCGCCGAAGTGATGAAGCCTGGCGCCTCCGTGA AGGTGTCCTGCAAGGCCTCCGGCTACAACTTCAAGGACACCTACATGGACTGGTG AAACAGACCCCTGAGCAGGGCCTGGAATGGATGGCGGATCGACCTGCCAACG GCGACTCCAAGTACGACCCTAAGTTCAGGGCAGAGTGACCATCACCGCCGACAC CTCCACCAACACCGCCTACATGGAAGTGTCTCCCTCGGTCTGAGGACACCGCC GTGTACTACTGCGCCAGGGCGGCATGATCTGTGACTTCGACGTGTGGGCCAGG GCACCAACGTGACAGTGTCTCTGGCGCCGAGGAGTGAGGTGGAGGATCTG GTGAGGCGGCTCCGAGATCGTGTGACCCAGTCTCTGCCACCATGTCCGTGTC TCCCGCGGAGAGGGCTACCTGTCTGTCTCCGCTCCCTCCCTCCCTCCCTCCAACT ACCTGCACTGGTATCAGCAGAAGCCTGGCTGCCCTCCCTCCCTGCTGATCTACCG GACCTCCAACCTGGCCTCTGGCATCCCCGACAGGTTCTCCGGCTGTGGCTCCGGC ACCGACTTCAACCTGACCATCTCCGGCTGGAAGCTGAGGACTTCGCCACCTACTA CTGCCAGCAGGGCTCCTCCCTGCTTACACCTTCGGACAGGGCACCAAGCTGGAA ATCAAG
40	940.	PM95A8 HL x l2C HL_codon optimized	artificial	nt	CAGGTGCAGCTGGTCCAGTCTGGCGCCGAAGTGATGAAGCCTGGCGCCTCCGTGA AGGTGTCCTGCAAGGCCTCCGGCTACAACTTCAAGGACACCTACATGGACTGGTG AAACAGACCCCTGAGCAGGGCCTGGAATGGATGGCGGATCGACCTGCCAACG GCGACTCCAAGTACGACCCTAAGTTCAGGGCAGAGTGACCATCACCGCCGACAC CTCCACCAACACCGCCTACATGGAAGTGTCTCCCTCGGTCTGAGGACACCGCC GTGTACTACTGCGCCAGGGCGGCATGATCTGTGACTTCGACGTGTGGGCCAGG GCACCAACGTGACAGTGTCTCTGGCGCCGAGGAGTGAGGTGGAGGATCTG

55					GTGAGGGGCTCCGAGATCGTGCTGACCCAGTCTCCTGCCACCATGTCCGTGTC TCCGGGAGAGGGCTACCTGTCTGCTCCGCTCCGCTCCTCCATCTCCTCCAACT ACCTGCACTGGTATCAGCAGAACCTGGCTCCCTCCTCGGCTGTGATCTACCG GACCTCAAACCTGGCTCTGGCATCCCGACAGGTTCTCCGGCTGTGGCTCCGGC ACCGACTTCAACCTGACCATCTCCGGCTGGAAGCTGAGGACTTCGCCACCTACTA CTGCCAGCAGGGCTCCTCCCTGCTTACACCTTCGACATTCGACAGGACCAAGCTGAA ATCAAGTCTGGCGAGGGGCTCTGAAGTGACGTGGTGGAAGCGGAGGGGA CTGTGACGCCCGGGGAAGTCTGAAGCTGTCTGTCCGCCAGCGGCTTTACCT TCAACAAGTACGCCATGAATTGGTCCGACAGGCCCGGAGGAAAGGCTGGAATG GGTGGCAGGATCCGGTCCAAGTACAACAACACTACGCCACCTACTACGCTGACTCCG TGAAGGACAGATTACCATCAGCCGGGACGACTCTAAGAACACCGCTATCTGCAG ATGAACAACCTGAAAACCGAGGATACAGCTGTGTACTATTGTGTGCGGCACGGCAA CTTCGGCAACTCCTACATCTCTACTTGGCCTATTGGGACAGGGAACACTGGTCA CCGTGTCTAGCGGAGGTGGCGAAGTGGGGAGGCGGATCTGCCAGCGGCAACCGT CCAGACCGTGGTACCCAGGAACCTTCCCTGACCGTCTCCAGCGGCAACCGT GACCTGACCTGTGGCTCCTTACCGGGCTGTGACCTCCGGCAACTACCTAACT GGTGCAGCAGAAACCCGACAGGCTCTAGAGGCTGTAGCGGCGCACCAAGTT TCTGGCCCTGGCACCCCTGCCAGATTCTCCGGCTCCCTGCTGGAGGCAAGCC GCTCTGACCTGTCTGGCGTGCAGCTGAGGACGAGGCGGAGTACTGTGTGC TGTGTTACTCCAACAGATGGGTCTCGGAGCGGCGCAAAAGCTGACCGTGTCTG
941.	PM07A12-H	artificial	aa		QVQLVESGGGLVKGPGSLRLSCAASGFTFSDYMSWVRQAPGKGLEWVASISDGSN TYSDIIKGRFTISRDNKNNLYQMNSLRAREDYAVYCARGFLLRHGAFDYWGQGT LVTSS
942.	PM07A12-HCDR1	artificial	aa		DYMS
943.	PM07A12-HCDR2	artificial	aa		SISDGGSNYYSDIIKG
944.	PM07A12-HCDR3	artificial	aa		GFPLLRHGAFDY
945.	PM07A12-H	artificial	nt		CAGGTGCAGCTGGTTCGAGTCTGGCGGCGGACTGGTGAAGCCTGGCGGGTCCCTG AGGCTGTCTGTGCCGCTCCGGCTTACCTTCTCCGACTACTACATGAGCTGGT CCGCCAGGCCCTGGGAAGGGCTGGAATGGTGGCTCCATCTCCGACGGCGG CTCCAACACCTACTACTCCGACATCATCAAGGCGCGGTTCAACATCTCCCGGACA ACGCCAAGAACAACTGTACCTGCAGATGAATCCCTGAGGCGCGGACACCGC CGTGTACTACTGCGCCCGGGCTTCCCTCTGCTGAGACACGCGGCTTCGATTACT GGGCGCAGGCAACCTGGTCAACCTCTCTCA
946.	PM07A12-L	artificial	aa		DIQMTQSPSSLSASVGDRVTITCRASQNVDTNVAWYQQKPGQAPKSLIYSATRYSDV PSRFGSGASGTDFTLTISVQSEDFATYYCQQYNSPYTFGGGTKLEIK
947.	PM07A12-LCDR1	artificial	aa		RASQNVDTNVA

948.	PM07A12-LCDR2	artificial	aa	SATYRS	GACATCCAGATGACCCAGTCCCCCAGCTCCCTGTCCGCTCCGTCGGCGACAGAG
949.	PM07A12-LCDR3	artificial	aa	QQNSYPYT	TGACCATCACCTGCAGGGCTCCAGAACGTGGACACCAACGTGGCTGGTATCA
950.	PM07A12-L	artificial	nt		GCAGAACCCGGCCAGGCCCTAAGTCCCTGATCTACTCCGCCACCTACCGGTAC TCTGACGTGCCTTCCCGTTCTCCGCTCCGCTCCGCTCCGACACGACTTCACCCCTGA CCATCTCAGCGTGCAGTCTGAGACTTCGCCACGTACTACTGCCAGCAGTACAAC TCCTACCTTACACCTTCGGCGGAGGACCAAGCTGGAATCAAG
951.	PM07A12-HL	artificial	aa		QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYMSWVRQAPGKLEWVASISDGGSN TYSDIIKGRFTISRDNAKNNLYQMNSLRAEDTAVYCARGFPLLRHGAFDYWGQTL VTVSSGGGGSGGGGGSDIQMTQSPSSLSASVGDRTITCRASQNVDTNVAWY QQKPGQAPKSLIYSATYRSDVPSRFSGSASGDTFTLISSVQSEDFATYYCQYNSYP YTFGGGTKLEIK
952.	PM07A12-HL	artificial	nt		CAGGTGCAGCTGGTTCGAGTCTGGCGGCGGACTGGTGAAGCCTGGCGGTCCTG AGGCTGTCTGTGCGCCTCGGCTTCACCTTCTCCGACTACTACATGAGCTGGGT CCGCCAGGCCCTGGGAAGGGCTGGAATGGTGGCTCCATCTCCGACGGCGG CTCCAACACTACTACTCCGACATCATCAAGGGCCGTTCAACATCTCCCGGACA ACGCCAAGAACAATCTGTACCTGCAGATGAATCCCTGAGCGCCGAGACACCGC CGTGTACTACTGCGCCCGGGCTTCCCTCTGCTGAGACGGCGCTTCGATTACT GGGCCAGGGCACCTGGTCACTCTCTCCTCAGTGGTGGTCTTGGCGCGG GCGGCTCCGGTGGTGGTCTGACATCCAGATGACCCAGTCCCGCAGCTCCCT GTCCGCTCCGTGGCGACAGAGTGACCATCACCTGCAGGGCTCCAGAACGTG GACACCAACGTGGCTGGTATCAGCAGAACCCCGCGGCGCTTAAGTCCCTGA TCTACTCCGCCACCTACCGGTACTCTGACGTGCCTTCCCGGTTCTCCGCTCCGCG TCGGCACCGACTTACCCCTGACCATCTCCAGCTGCAGTCTGAGGACTTCGCCAC GTACTACTGCCAGCAGTACAACCTCCTACCCCTACACCTTCGGCGGAGGACCAAGC TGGAAATCAAG
953.	PM07A12 HL X I2C HL	artificial	aa		QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYMSWVRQAPGKLEWVASISDGGSN TYSDIIKGRFTISRDNAKNNLYQMNSLRAEDTAVYCARGFPLLRHGAFDYWGQTL VTVSSGGGGSGGGGGSDIQMTQSPSSLSASVGDRTITCRASQNVDTNVAWY QQKPGQAPKSLIYSATYRSDVPSRFSGSASGDTFTLISSVQSEDFATYYCQYNSYP YTFGGGTKLEIKSGGGSEVQLVESGGGLVQPGGSLKSCAASGFTFNKYAMNWRQ APGKLEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNLLKTEDTAVYY CVRHGNFGNSYISYWAYWGQGLTVTVSSGGGGSGGGGGSTVVTQEPSTVS PGGTVTLTCCGSTGAVTSGNYPNWWQKPGQAPRGLIGGKFLAPGTPARFSGSLG GKAALTSGVQPEDEAEYYCVLWYSNRWVFGGGTKLTVL

954.	PM07A12 HL X I2C HL	artificial	nt	<p>CAGGTGCAGCTGGTCGAGTCTGGCGGGGACTGGTGAAGCCTGGCGGGTCCCTG AGGTGTCTGTGCCGCTCCGGCTTACCTTCTCCGACTACTACATGAGCTGGT CGCCAGGCCCTGGGAAGGGCTGGAATGGTGCCCTCATCTCCGACGGCGG CTCCAACACCTACTCTCCGACATCATCAAGGGCCGTTACCATCTCCCGGGACA AGCCAAAGAACAATCTGACCTGCAGATGAATCCCTGAGGGCCGAGACACCGC CGTGTACTACTGCGCCCGGGCTTCCCTCTGCTGAGACACGGCGCTTCGATTACT GGGCCAGGGCACCTGGTACCGCTCTCCTCAGTGGTGGTGTCTGGCGGG GCGGCTCCGGTGGTGGTCTGACATCCAGATGACCCAGTCCCCAGCTCCCT GTCGCTCCGTGGCGACAGAGTGACCATCACCTGCAGGGCCCTCCAGAACGTG GACACCAACGTGGCTGGTATCAGCAGAGCCCGGCCAGGCCCTAAGTCCCTGA TCTACTCCGCCACCTACCGGTACTCTGACGTGCTTCCGGTCTCCGGCTCCGG TCGGCACCGACTTACCTGACCATCTCCAGCTCCAGCTGAGTCTGAGACTTCGCCAC GTACTACTGCCAGCAGTACAACCTCTACCTTACACCTTCGGCGGAGGACCAAGC TGGAAATCAAGTCCGGAGGTGGTGGATCCGAGGTGCAGCTGGTCGAGTCTGGAGG AGGATTGGTGAGCTGGAGGGTCAATTGAACCTCTCATGTGCAGCCTCTGGATTCA CCTTCAATAAGTACGCCATGAACCTGGTCCGCCAGGCTCCAGGAAAGGTTGGAA TGGGTGCTCGCATAGAAGTAAATATAATATTGCAACATATTATGCCGATTCAAG TGAAGACAGGTTACCATCTCCAGAGATGATTCAAAAACACATGCCATCTACAAA TGAACAACTTGAACACTGAGGACACTGCCGTACTACTGTGAGACATGGGAAC TTCGGTAATAGCTACATCTCTACTGGGCTTACTGGGCCAAGGACTCTGGTCAC CGTCTCCTCAGGTGGTGGTCTGGCGGGCGGCTCCGGTGGTGGTGGTCT CAGACTGTTGTGACTCAGGAACCTTCACTCACCGTATCACCTGGTGGAAACAGTCAC ACTCACTTGTGGCTCCTCGACTGGGCTGTACATCTGGCAACTACCCAAACTGGG TCCAACAAAACCAGGTACGGCACCCGTGTCTAATAGTGGACTAAGTTCCCTC GCCCGGGTACTCTGCCAGATTCTCAGGCTCCCTGCTTGGAGGCAAGGCTGCC TCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAAGATATTACTGTGTTCTATGG TACAGCAACCGCTGGGTGTTCCGTGGAGGAACCAACTGACTGTCTCTA</p>
955.	PM07A12-H codon optimized	artificial	nt	<p>CAGGTGCAGCTGGTCGAGTCTGGCGGGGACTGGTCAAGCCTGGCGGGTCCCTG AGACTGTCTTGGCTGCCCTCCGGCTTACCTTCTCCGACTACTACATGTCTGGGT CGCCAGGCTCCTGGCAAGGGACTGGAATGGTGCCCTCCATCTCCGACGGCGG CTCCAACACCTACTACTCCGACATCATCAAGGGCCGTTACCATCTCCAGGGACA ACGCTAAGAACAACCTGTACCTGCAGATGAATCCCTGAGGGCCGAGACACCGC CGTGTACTACTGCGCCAGGGCTTCCCACTGCTGAGACACGGCGCTTCGATTACT GGGCCAGGGCACCTGGTCAACAGTGTCTCT</p>
956.	PM07A12-L codon optimized	artificial	nt	<p>GACATCCAGATGACCCAGTCCCACTCCCTGCTGCCCTGGCGGACAGAGT GACCATCACATGCCCGGGCTCCCAAGAACGTGGACACCAACCGTGGCATGGTATCAG</p>

5	957.	PM07A12-HL codon optimized	artificial	nt	<p>CAGAGCCAGGCGGCCCCCTAAGTCCCTGATCTACTCTGTCACCTACCGGTACTC CGACGTGCCCTCCAGGTTCTGTGGCTCCGCCCTGGCACCAGATTACCCCTGACCA TCTCTCCGTGCAGTCCGAGGACTTCGCTACCTACTACTGCCAGCAGTACAACTCC TACCCCTACACCTTCGGCGGAGGCACCAAGCTGGAATCAAG</p> <p>CAGGTGCAGCTGGTCGAGTCTGGCGGCGGACTGGTCAAGCCTGGCGGCTCCCTG AGACTGTCTTGGCGTCCCTCCGGCTTCACTTCTCCGACTACTACATGTCTCTGGT CCGCCAGGCTCCTGGCAAGGACTGGAATGGTGGCTCCATCTCCGACGGCGG CTCCAACACTACTACTCCGACATCATCAAGGCGGTTTACCATCTCCAGGGACA ACGCTAAGAACAACTGTACCTGCAGATGAATCCCTGAGGCCGAGACACCGC CGTGTACTACTGCCCAGGGCTTCCCACTGCTGAGACACGGGCGCTTCGATTACT GGGCCAGGGCACCTTGGTCACAGTGTCTCTGGCGGAGGGCGGAAGTGGAGCGG GAGGAAGCGGAGGGCGGATCCGACATCCAGATGACCCAGTCCCATCTCCCT GTCTGCCCTCCGTGGCGACAGAGTGACCATCACATGCCGGGCTCCAGAACGTG GACACCAACGTGGCATGGTATCAGCAGAAGCCAGGCCAGGCCCTAAGTCCCTGA TCTACTCTGCCACCTACCGGTACTCCGACGTGCCCTCCAGGTTCTGTGGTCCGCG TCTGGCACCGACTTCACTGACCATCTCTCCGTGACGTCGAGGACTTCGCTAC CTACTACTGCCAGCAGTACAACCTCTACCTTACACCTTCGCGCGAGGACCAAGC TGGAAATCAAG</p>
10					<p>CAGGTGCAGCTGGTCGAGTCTGGCGGCGGACTGGTCAAGCCTGGCGGCTCCCTG AGACTGTCTTGGCGTCCCTCCGGCTTCACTTCTCCGACTACTACATGTCTCTGGT CCGCCAGGCTCCTGGCAAGGACTGGAATGGTGGCTCCATCTCCGACGGCGG CTCCAACACTACTACTCCGACATCATCAAGGCGGTTTACCATCTCCAGGGACA ACGCTAAGAACAACTGTACCTGCAGATGAATCCCTGAGGCCGAGACACCGC CGTGTACTACTGCCCAGGGCTTCCCACTGCTGAGACACGGGCGCTTCGATTACT GGGCCAGGGCACCTTGGTCACAGTGTCTCTGGCGGAGGGCGGAAGTGGAGCGG GAGGAAGCGGAGGGCGGATCCGACATCCAGATGACCCAGTCCCATCTCCCT GTCTGCCCTCCGTGGCGACAGAGTGACCATCACATGCCGGGCTCCAGAACGTG GACACCAACGTGGCATGGTATCAGCAGAAGCCAGGCCAGGCCCTAAGTCCCTGA TCTACTCTGCCACCTACCGGTACTCCGACGTGCCCTCCAGGTTCTGTGGTCCGCG TCTGGCACCGACTTCACTGACCATCTCTCCGTGACGTCGAGGACTTCGCTAC CTACTACTGCCAGCAGTACAACCTCTACCTTACACCTTCGCGCGAGGACCAAGC TGGAAATCAAGTCCGCGGAGGGGCTCTGAAGTGCAGCTGGTGGAAAGCGGAG GGGGACTGGTGACGCCCGGGGGAAGTCTGAAGCTGTCTGTGCCGCCAGCGGCT TTACCTTCAACAAGTACGCCATGAATTGGTCCGACAGGCCCGGGAAGGCGCTG GAATGGTGGCACGGATCCGGTCCAAAGTACAACAACTACGCCACCTACTACGCTGA CTCCGTGAAGGACAGATTACCATCAGCCGGGACGACTCTAAGAACACCGGCTATC</p>
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55	958.	PM07A12 HL x I2C HL codon optimized	artificial	nt	<p>CAGGTGCAGCTGGTCGAGTCTGGCGGCGGACTGGTCAAGCCTGGCGGCTCCCTG AGACTGTCTTGGCGTCCCTCCGGCTTCACTTCTCCGACTACTACATGTCTCTGGT CCGCCAGGCTCCTGGCAAGGACTGGAATGGTGGCTCCATCTCCGACGGCGG CTCCAACACTACTACTCCGACATCATCAAGGCGGTTTACCATCTCCAGGGACA ACGCTAAGAACAACTGTACCTGCAGATGAATCCCTGAGGCCGAGACACCGC CGTGTACTACTGCCCAGGGCTTCCCACTGCTGAGACACGGGCGCTTCGATTACT GGGCCAGGGCACCTTGGTCACAGTGTCTCTGGCGGAGGGCGGAAGTGGAGCGG GAGGAAGCGGAGGGCGGATCCGACATCCAGATGACCCAGTCCCATCTCCCT GTCTGCCCTCCGTGGCGACAGAGTGACCATCACATGCCGGGCTCCAGAACGTG GACACCAACGTGGCATGGTATCAGCAGAAGCCAGGCCAGGCCCTAAGTCCCTGA TCTACTCTGCCACCTACCGGTACTCCGACGTGCCCTCCAGGTTCTGTGGTCCGCG TCTGGCACCGACTTCACTGACCATCTCTCCGTGACGTCGAGGACTTCGCTAC CTACTACTGCCAGCAGTACAACCTCTACCTTACACCTTCGCGCGAGGACCAAGC TGGAAATCAAGTCCGCGGAGGGGCTCTGAAGTGCAGCTGGTGGAAAGCGGAG GGGGACTGGTGACGCCCGGGGGAAGTCTGAAGCTGTCTGTGCCGCCAGCGGCT TTACCTTCAACAAGTACGCCATGAATTGGTCCGACAGGCCCGGGAAGGCGCTG GAATGGTGGCACGGATCCGGTCCAAAGTACAACAACTACGCCACCTACTACGCTGA CTCCGTGAAGGACAGATTACCATCAGCCGGGACGACTCTAAGAACACCGGCTATC</p>

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				TGCAGATGAACAACCTGAAACCGAGGATACAGCTGTGACTATTGTGTGCGGCAC GGCAACTTCGGCAACTCCTACATCTCCTACTGGCCCTATTGGGACAGGGAACACT GGTACCGTGTCTAGCGGAGGTGGCGAAGTGGGAGGCGGATCTGGCGGTGG CGATCCAGACCGTGGTCAACAGGAACCTTCCTGACCGTCTCCCGAGCGGC ACCGTACCCCTGACCTGTGGCTCCTACCGCGCTGTGACCTCCGGCAACTACC CTAAGTGGGTGACGAGAAACCGGACAGGCTCCTAGAGGCTGAGCGCGGCAC CAAGTTCTGGCCCTGGCACCCCTGCCAGATTCTCCGGCTCCCTGCTGGGAGGC AAGGCCGCTCTGACCCCTGTCTGGCGTGCAGCCTGAGGACGAGGCCGAGTACTACT GTGTGCTGTGGTACTCCAAACAGATGGGTTCGGAGCGGCGCAAAAGCTGACCGT GCTG
959.	PM07F8-H	artificial	aa	QVQLVESGGGLVQPGESLRSLSCAASGFTFSYYMSWVRQAPGKGLEWVASISDGGSN TYYSDIKGRFTISRDNNAKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAFDYWGQGT LTVSS
960.	PM07F8-HCDR1	artificial	aa	DYYMS
961.	PM07F8-HCDR2	artificial	aa	SISDGGSNYYSDIIKG
962.	PM07F8-HCDR3	artificial	aa	GFPLLRHGAFDY
963.	PM07F8-H	artificial	nt	CAGTGCAGCTGGTGCAGTCTGGCGGCGGACTGGTGAAGCTGGCGAGTCCCTG AGCGTGTCTGTCCGCTCCGCTCCGCTTCACTTCCGACTACTACATGAGCTGGGT CCGCCAGGCCCTGGGAAGGGCTGGAATGGTGGCTCCATCTCCGACGGCGG CTCCAACACCTACTACTCCGACATCATCAAGGGCCGGTTCAACATCTCCCGGACA ACGCCAAGAACAGCCTGTACCTGCAGATGAATCCCTGAAGGCCGAGGACACCCGC CGTGTACTACTGCGCCCGGGCTTCCCTCTGCTGAGACAGGCGGCTTCGATTACT GGGCCAGGGCACCCCTGGTCAACCGTCTCCTCA
964.	PM07F8-L	artificial	aa	DIQMTQSPSSLSASVGRVTITCRASQNVDTNVAWYQQKPGQAPKSLIYSATYRSDV PSRFGSGASGDTFTLTISVQSEDFATYYCQYNSYPYTFGGGKLEIK
965.	PM07F8-LCDR1	artificial	aa	RASQNVDTNVA
966.	PM07F8-LCDR2	artificial	aa	SATYRYS
967.	PM07F8-LCDR3	artificial	aa	QQYNSYPY
968.	PM07F8-L	artificial	nt	GACATCCAGATGACCCAGTCCCCAGCTCCCTGTCCGCTCCGTGGCGGACAGAG TGACCATCACCTGCAGGGCTCCAGAACGTTGACACCAACGTTGGCTGGTATCA GCAGAAGCCCGGCCAGGCCCTAAGTCCCTGATCTACTCCGCCACCTACCGGTAC TCTGACGTGCTTCCCGGTTCTCCGGCTCCGCTCCGCGACCCGACTTCAACCTGA CCATCTCCAGCGTGCAGTCTGAGGACTTCCGCGCTACTACTGCCAGCAGTACAAC TCCTACCCCTTACACCTTCGGCGGAGGGACCAAGCTGGAATCAAG
969.	PM07F8-HL	artificial	aa	QVQLVESGGGLVQPGESLRSLSCAASGFTFSYYMSWVRQAPGKGLEWVASISDGGSN TYYSDIKGRFTISRDNNAKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAFDYWGQGT LTVSS

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973.	PM07F8-H codon optimized	artificial	nt		<p>CAGGTGCAGTGGTCGAGTCTGGCGGAGTGGTCAAGCCTGGCGAGTCCCTGA GACTGCTTGGCTCCGCTCCGCTTCACTTCTCGGACTACTACATGCTCGGTC CGCCAGGCTCCTGGCAAGGAGTGGATGGTGGCTCCATCTCCGAGCGGCT CCAACACCTACTACTCCGACATCATCAAGGGCCGTTACCATCTCCAGGGACAAC GCCAAGAACTCCCTGTACCTGCAGATGAAGTCCCTGAAGGCCGAGACACCGCCG TGTAATACTGCGCCAGGGCTTCCCACTGCTGAGACACGGCGCTTCGATTACTGG GGCAGGGCACCTGGTCAAGTCTCT</p>
974.	PM07F8-H codon optimized	artificial	nt		<p>GACATCCAGATGACCCAGTCCCATCTCCCTGCTGCTCCGTGGCGACAGAT GACCATCATATGCCGGGCTCCAGAACGTTGACACCAACGTTGGCATGGTATCAG CAGAAGCCAGGCCAGGCCCTAAGTCCCTGATCTACTTCCACCTACCGGTACTC CGACGTGCCCTCCAGGTTCTCTGGCTCCGCTCTGGCACCGACTTCACTGACCA TCTCTCCGTGCAGTCCGAGGACTTCCGCTACTACTGCTGACGAGTACAACCTCC TACCCCTACACCTTCCGGGAGGCCACCAAGCTGGAATCAAG</p>
975.	PM07F8-H codon optimized	artificial	nt		<p>CAGGTGCAGTGGTGCAGTCTGGCGGAGTGGTCAAGCCTGGCGAGTCCCTGA GACTGCTTGGCTCCGCTCCGCTTCACTTCTCGGACTACTACATGCTCGGTC CGCCAGGCTCCTGGCAAGGAGTGGATGGTGGCTCCATCTCCGAGCGGCT CCAACACCTACTACTCCGACATCATCAAGGGCCGTTCACTCTCCAGGGACAAC GCCAAGAACTCCCTGTACCTGCAGATGAAGTCCCTGAAGGCCGAGACACCGCCG TGTAATACTGCGCCAGGGCTTCCCACTGCTGAGACACGGCGCTTCGATTACTGG</p>

55	976.				GGCCAGGGCACCCCTGGTCAAGTGTCTCTGGCGGAGGGGGAAGTGGAGGGGA GGAAGCGGAGCGGGGATCCGACATCCAGATCCAGATGACCCAGTCCCCATCCTCCCTGT CTGCCTCCGTGGGACAGAGTGACCATCACATGCCGGGCTCCCGAAGCGTGA CACCAACGTGGCATGGTATCAGCAGAAGCCAGGCCAGGCCCTAAGTCCCTGATC TACTTGCCACCTACCGGTACTCCGACGTGCCCTCCAGGTTCTCTGGCTCCGCCCTC TGGCACCGACTTCACCCCTGACCATCTCTCCGTGCAGTCCGAGGACTTCGCTACCT ACTACTGCCAGCAGTACAACTCCTACCCCTTACACCTTCGGCGGAGGCACCAAGCTG GAAATCAAG
50	PM07F8 HL x I2C HL codon optimized	artificial	nt		CAGGTGCAGCTGGTCGAGTCTGGCGGCGGACTGGTCAAGCCTGGCGAGTCCCTGA GACTGTCTTGGCTGCCCTCCGGCTTACACCTTCTCCGACTACTACATGTCTCTGGTC CGCCAGGCTCCTGGCAAGGACTGGAATGGTGGCTCCATCTCCGACGGCGGCT CCAACACCTACTACTCCGACATCATCAAGGGCCGTTACCATCTCCAGGACAAAC GCCAAGAACTCCCTGTACCTGCAGATGAACCTCCCTGAAGCCGAGGACACCCGCCG TGTACTACTGCCCGAGGGCTTCCCACTGCTGAGACACGGCCCTTCGATTACTGG GGCCAGGGCACCCCTGGTCAAGTGTCTCTGGCGGAGGCGGAAGTGGAGGCGGA GGAAGCGGAGGCGGCGATCCGACATCCAGATCCAGATGCCAGTCCCATCCTCCCTGT CTGCCTCCGTGGGACAGAGTGACCATCACATGCCGGGCTCCCGAAGCGTGA CACCAACGTGGCATGGTATCAGCAGAAGCCAGGCCAGGCCCTAAGTCCCTGATC TACTCTGCCACCTACCGGTACTCCGACGTGCCCTCCAGGTTCTCTGGCTCCGCCCTC TGGCACCGACTTACCCCTGACCATCTCTCCGTGCAGTCCGAGGACTTCGCTACCT ACTACTGCCAGCAGTACAACTCCTACCCCTTACACCTTCGGCGGAGGCACCAAGCTG GAAATCAAGTCCGCGGAGGGGCTCTGAAGTGCAGTGGTGGAAAGCGGAGGG GGACTGGTGCAGCCCGGGGAAGTCTGAAGCTGTCTGTGCCGCCAGCGGCTTTA CCTTCAACAAGTACGCCATGAATTGGTCCGACAGGCCCGCCAGGGAAGGCCCTGA ATGGGTGGCACGGATCCGTCCAAAGTACAACTACGCCACCTACTACGCTGACT CCGTGAAGGACAGATTACCATCAGCCGGGACGACTCTAAGAACACCGCCTATCTG CAGATGAACAACCTGAAACCCGAGGATACAGTGTGACTATTGTGTGGGCACGG CAACTTCGGCAACTCCTACATCTCTACTGGCCCTATTGGGACAGGGAACACTGG TCACCGTGTCTAGCGGAGGTGGCGGAAGTGGGGAGGCGGATCTGGCGGTGGCG GATCCAGACCGTGGTCAACCCAGGAACCTTCCCTGACCGTCTCCCGAGGGGCAC CGTGACCCCTGACCTGTGGCTCCTACCGGGGCTGTGACCTCCGGCAACTACCTA ACTGGGTGCAGCAGAAACCCGACAGGCTCTAGAGGCCCTGATCGGGGACCAAA GTTTCTGGCCCTTGCCACCCCTGCCAGATTCTCCGGCTCCCTGCTGGAGGCAAG GCCGCTCTGACCCCTGTCTGGCTGCAGCCTGAGGACGAGGCCGCTACTACTGTG TGCTGTGTTACTCCAAACAGATGGGTCTTCGGAGGCGGCACAAAGCTGACCGTGT
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977.	PM07E5-H	artificial	aa	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYMSWVRQAPGKGLEWVASISDGGSN TYSYSDIIKGRFTISRDNNAKNNLYQMNSLRAEDTAVYYCARGFPLLRHGAIDYWGQGT LTVSS
978.	PM07E5-HCDR1	artificial	aa	DYYMS
979.	PM07E5-HCDR2	artificial	aa	SISDGGSNYYSDIIKG
980.	PM07E5-HCDR3	artificial	aa	GFPLLRHGAIDY
981.	PM07E5-H	artificial	nt	CAGGTGCAGCTGGTCGAGTCTGGCGGGGACTGGTGAAGCCTGGCGGGTCCCTG AGGCTGTCTGTGCGCGCTCGGCTTCACTTCTCCGACTACTACATGAGCTGGT CGCCAGGCCCTGGGAAGGGCTGGAATGGTGGCTCCATCTCCGACGGCGG CTCCAACACCTACTACTCCGACATCATCAAGGCCGGTTCACCATCTCCGAGACA ACGCCAAGAACAATCTGTACCTGCAGATGAATCCCTGAGGCCGAGGACACCGC CGTGTACTACTGCGCCCGGGCTTCCCTCTGCTGAGACACGGCGGCATCGATTACT GGGCCAGGGCACCTGGTCACCGTCTCCTCA
982.	PM07E5-L	artificial	aa	DIQMTQSPSSLSASVGDRTITCRASQNVDTNVAWYQQKPGQAPKSLIYSATYRYS PSRFGSASGTDFTLTISVQSEDFATYCCQYNISYPYTFGGGKLEIK
983.	PM07E5-LCDR1	artificial	aa	RASQNVDTNVA
984.	PM07E5-LCDR2	artificial	aa	SATYRYS
985.	PM07E5-LCDR3	artificial	aa	QQYNSYPYT
986.	PM07E5-L	artificial	nt	GACATCCAGATGACCCAGTCCCCAGCTCCCTGCGCCTCCGTGGCGACAGAG TGACCATCACCTGCAGGGCTCCAGAACGTGGACACCAACGTGGCCTGGTATCA GCAGAACCCCGCCAGGCCCTAAGTCCCTGATCTACTCCGCCACCTACCGGTAC TCTGACGTGCCCTCCCGGTTCTCCGGCTCCCGTCCGGCACCCGACTTCACCCCTGA CCATCTCCAGCGTGCAGTCTGAGGACTTCGCCACGCTACTGCCAGCAGTACAAC TCCTACCTTACACCTTCGGCGGAGGACCAAGCTGGAATCAAG
987.	PM07E5-HL	artificial	aa	QVQLVESGGGLVKPGGSLRLSCAASGFTFSDYMSWVRQAPGKGLEWVASISDGGSN TYSYSDIIKGRFTISRDNNAKNNLYQMNSLRAEDTAVYYCARGFPLLRHGAIDYWGQGT LTVSSGGGGGGGGGGGSDIQMTQSPSSLSASVGDRTITCRASQNVDTNVAWY QQKPGQAPKSLIYSATYRYSVPSRFGSASGTDFTLTISVQSEDFATYCCQYNISYP YTFGGGKLEIK
988.	PM07E5-HL	artificial	nt	CAGGTGCAGCTGGTCGAGTCTGGCGGGGACTGGTGAAGCCTGGCGGGTCCCTG AGGCTGTCTGTGCGCGCTCCGGCTTCACTTCTCCGACTACTACATGAGCTGGT CGCCAGGCCCTGGGAAGGGCTGGAATGGTGGCTCCATCTCCGACGGCGG CTCCAACACCTACTACTCCGACATCATCAAGGCCGGTTCACCATCTCCGAGACA ACGCCAAGAACAATCTGTACCTGCAGATGAATCCCTGAGGCCGAGGACACCGC CGTGTACTACTGCGCCCGGGCTTCCCTCTGCTGAGACACGGCGGCATCGATTACT GGGCCAGGGCACCTGGTCACCGTCTCCTCAGGTGGTGGTCTTGCGCGGG

989.	PM07E5 HL X I2C HL	aa artificial
		nt artificial
		PM07E5 HL X I2C HL

				CGTCTCCTCAGGTGGTGGTGTCTGGCGGCGGCTCCGGTGGTGGTGGTCT CAGACTGTGTGACTCAGGAACCTTCACTCACCCTATCACCTGGTGAACAGTCAC ACTCACTTGTGGCTCCTCGACTGGGCTGTACATCTGGAACCTACCAAACTGGG TCCAACAAAACAGGTGAGGACCCCGTGGTCTAATAGGTGGGACTAAGTTCTC GCCCGGTACTCTGCCAGATTCTCAGGCTCCCTGCTGGAGGCAAGGCTGCC TCACCTCTCAGGGGTACAGCCAGAGGATGAGGCAAGATATTACTGTGTTCTATGG TACAGCAACCGCTGGGTGTTGGTGAGGAACCAAACTGACTGTCTCTA
991.	PM07D3-H	artificial	aa	QVQLVESGGGLVKPGESLRSCAASGFTFSDYMSWVRQAPGKGLEWVASISDGGSN TYYSDIKGRFTISRDNNAKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAIDYWGQGTLY TVSS
992.	PM07D3-HCDR1	artificial	aa	DYMS
993.	PM07D3-HCDR2	artificial	aa	SISDGGSNYYSDIIG
994.	PM07D3-HCDR3	artificial	aa	GFPLLRHGAIDY
995.	PM07D3-H	artificial	nt	CAGGTGCAGCTGGTTCGAGTCTGGCGGCGGACTGGTGAAGCCTGGCGAGTCCCTG AGGCTGTCTGTGGCGGCTCCGGCTTCACTTCTCCGACTACTACATGAGCTGGGT CCGCCAGGCCCTGGGAAGGGCTGGAATGGGTGGCTCCATCTCCGACGGCGG CTCCAACACCTACTACTCCGACATCATCAAGGCGCGGTTCAACATCTCCCGAGACA ACGCCAAGAACAGCCTGTACTCGAGATCACTCCCTGAAGGCCGAGGACACCGC CGTGTACTACTGCCCGCGGGCTTCCCTCTGCTGAGACACGGCGCCATCGATTACT GGGCCAGGGCACCTGGTCACCGTCTCTCA
996.	PM07D3-L	artificial	aa	DIQMTQSPSSLSASVGDRTVITCRASQNVDTNVAWYQQKPGQAPKSLIYSATYRSDV PSRFSGSASGTDFLTLSISVQSEDFATYQCQYNSYPYTFGGGTKLEIK
997.	PM07D3-LCDR1	artificial	aa	RASQNVDTNVA
998.	PM07D3-LCDR2	artificial	aa	SATYRYS
999.	PM07D3-LCDR3	artificial	aa	QQYNSYPY
1000.	PM07D3-L	artificial	nt	GACATCCAGATGACCCAGTCCCCAGCTCCCTGTCCGCCTCCGTGGCGGACAGAG TGACCATCACCTGCAGGGCTCCCAAGAACGTGGACACCAACGCTGGCCTGGTATCA GCAGAAGCCCGCCAGGCCCTTAAGTCCCTGATCTACTCCGCCACCTACCGGTAC TCTGACGTGCTTCCCGGTTCTCCGGCTCCGGCTCCGGCAGCCGACTTCAACCTGA CCATCTCCAGCGTGCAGTCTGAGGACTTCGCCACGTACTACTGCCAGCAGTACAAC TCCTACCTTACACCTTCGGCGGAGGGACCAAGCTGGAATCAAG
1001.	PM07D3-HL	artificial	aa	QVQLVESGGGLVKPGESLRSCAASGFTFSDYMSWVRQAPGKGLEWVASISDGGSN TYYSDIKGRFTISRDNNAKNSLYLQMNSLKAEDTAVYYCARGFPLLRHGAIDYWGQGTLY TVSSGGGSGGSGGSGGSDIQMTQSPSSLSASVGDRTVITCRASQNVDTNVAWYQ QKPGQAPKSLIYSATYRSDVPSRFSGSASGTDFLTLSISVQSEDFATYQCQYNSYPY TFGGGTKLEIK

1002.	PM07D3-HL	artificial	nt	<p>CAGGTGCAGCTGGTCGAGTCTGGCGGCGGACTGGTGAAGCCTGGCGAGTCCCTG AGGTGTCTGTGCGCCTCCGGCTTCACTTCTCCGACTACTACATGAGCTGGGT CCGCCAGGCCCTGGAAGGGCTGGAATGGTGGCTCCATCTCCGACGGCGG CTCCACACCTACTACTCCGACATCATCAAGGGCGGTTACCATCTCCCGAGACA ACGCCAAGAACAGCCTGTACCTGCAGATGAACCTCCCTGAAGCCGAGGACACCCG CGTGTACTACTGCGCCCGGGCTTCCCTCTGCTGAGACAGCGGCCATCGATTACT GGGCCAGGGCACCTGGTCAACGCTCCTCAGGTGAGTGGTGGTCTGGCGGCG GCGCTCCGGTGGTGGTCTGACATCCAGATGACCCAGTCCCCAGCTCCCT GTCGCTCCGTGGGACAGAGTGACCATCACTGCAGGCTCCAGAACGTG GACACCAACGTGGCTGGTATCAGCAGAACCCGCGGAGCCCTAAGTCCCTGA TCTACTCCGCCACCTACCGGTACTCTGACGTGCTTCCGGTCTCCGGCTCCGG TCGGCACCGACTTCACTTCACTTCCAGGTGACGTCTGAGGACTTCCGCAC GTACTACTGCCAGCAGTACAACCTCCTACCTTACACCTTCGGCGGAGGACCAAGC TGGAAATCAAG</p>
1003.	PM07D3 HL X I2C HL	artificial	aa	<p>QVQLVESGGGLVQPGESLRSCAASGFTFSYYMSWVRQAPGKGLEWVASISDGGSN TYSDIIKGRFTISRDNKNSLYLQMNSLKAEDTAVYYCARGFLLRHGAIDYWGQGLV TVSSGGGSGGGSGGSDIQMTQSPSSLSASVGRVITCRASQNVDTNVAWYQ QKPGQAPKSLIYSATYRSDVPSRFGSASGDTLTLSVQSEDFATYYCQYNSYPY TFGGGTKLEIKSGGGSEVQLVESGGGLVQPGSLKLSAASGFTFNKYAMNWRQA PGKLEWVARIRSKYNNYATYADSVKDRFTISRDDSKNTAYLQMNLLKTEDTAVYVC VRHGNFGNSIYSYWAYWGQGLTVTVSSGGGSGGGSGGSGTQVTPQEPSLTVSP GGTVTLTCSSTGAVTSGNYPNWWQKPGQAPRGLIGGTKFLAPGTPARFSGSLGG KAALTLSGVQPEDEAEYFCVLWYSNRWVFGGGLTLV</p>
1004.	PM07D3 HL X I2C HL	artificial	nt	<p>CAGGTGCAGCTGGTCGAGTCTGGCGGCGGACTGGTGAAGCCTGGCGAGTCCCTG AGGTGTCTGTGCGCCTCCGGCTTCACTTCTCCGACTACTACATGAGCTGGGT CCGCCAGGCCCTGGAAGGGCTGGAATGGTGGCTCCATCTCCGACGGCGG CTCCACACCTACTACTCCGACATCATCAAGGGCGGTTACCATCTCCCGAGACA ACGCCAAGAACAGCCTGTACCTGCAGATGAACCTCCCTGAAGCCGAGGACACCCG CGTGTACTACTGCGCCCGGGCTTCCCTCTGCTGAGACAGCGGCCATCGATTACT GGGCCAGGGCACCTGGTCAACGCTCCTCAGGTGAGTGGTGGTCTGGCGGCG GCGCTCCGGTGGTGGTCTGACATCCAGATGACCCAGTCCCCAGCTCCCT GTCGCTCCGTGGGACAGAGTGACCATCACTGCAGGCTCCAGAACGTG GACACCAACGTGGCTGGTATCAGCAGAACCCGCGGAGCCCTAAGTCCCTGA TCTACTCCGCCACCTACCGGTACTCTGACGTGCTTCCGGTCTCCGGCTCCGG TCGGCACCGACTTCACTTCACTTCCAGGTGACGTCTGAGGACTTCCGCAC GTACTACTGCCAGCAGTACAACCTCCTACCTTACACCTTCGGCGGAGGACCAAGC</p>

				TGGAATCAAGTCCGGAGGTGGTGGATCCGAGGTGCAGCTGGTGCAGTCTGGAGG AGGATTGGTGCAGCCTGGAGGGTCATTGAAACTCTCATGTGCAGCCTCTGGATTCA CCTTCAATAAGTACGCCATGAAGTGGTCCGCGCAGGCTCCAGGAAAGGTTTGAA TGGTTCCTCGCATAGAAGTAAATAATAATTAATGAACATATTATGCCGATTGAG TGAAGACAGGTTACCATCTCCAGAGATGATCAAAAACACTGCCATCTATACAAA TGAACAACTTGAAACTGAGGACACTGCCGTGTAATACTGTGTGAGACATGGGAAC TTCGGTAATAGCTACATATCTACTGGCTTACTGGGCGGCTCCGGTGGTGGTTCT CGTCTCCTCAGGTGGTGGTCTGGGCGGCGGCTCCGGTGGTGGTGGTGGTCT CAGACTGTTGTGACTCAGGAACCTTCACTCAGGATACCTGATCAGTGTGGAAACAGT ACTCACTTGTGGCTCCTCGACTGGGCTGTACATCTGCACTACCCAACTGGG TCCAACAAAACAGGTCAGGACCCCGTGGTCTAATAGGTGGACTAAGTTCTCTC GCCCGGTACTCTCCAGATTCTCAGGCTCCCTGTTGAGGCAAGCTGCC TCACCTCTCAGGGTACAGCAGAGGATGAGGCAAGATATTACTGTGTTCTATGG TACAGCAACCGCTGGGTGTTGGTGGAGGAACCAAACTGACTGTCTTA
1005.	PM26C9-H	artificial	aa	QVQLVQSGPEVKPGASVKVSKASGYTFTGYVMHWVRQTPGQRLEWIGYINPYNDV TRYNGKFKGRVTITSDKSSSTAYMELSSLRSEDTAVYYCARGENWYYFDSWGRGTLVT VSS
1006.	PM26C9-HCDR1	artificial	aa	GYVMH
1007.	PM26C9-HCDR2	artificial	aa	YINPYNDVTRYNGKFKG
1008.	PM26C9-HCDR3	artificial	aa	GENWYYFDS
1009.	PM26C9-H	artificial	nt	CAGGTGCAGCTGGTCCAGTCCGGCCCTGAGGTGGTGAAGCCTGGCGCTCCGTGA AGGTGTCCTGCAAGGCTCCGGCTACACCTTACCGGCTACGTGATGCACTGGT GAGACAGACACCCGGCCAGCGCTGGAATGGATCGGCTACATCAACCCCTTACAAC GAGTGACCCGGTACAACGGCAAGTTCAAGGGCAGAGTCAACATTACCAGCGACA AGTCTCTCCACCGCTACATGGAAGTGTCCAGCCTGAGGTCTGAGGACACCGC CGTGTACTACTGCGCCAGGGCGAGAACTGTTACTACTCGACTCCTGGGCGAGA GGCACTCTGTCACCGTCTCCTCC
1010.	PM26C9-L	artificial	aa	DVMTQSPLSLAVTLGQPASISCRASESIDSYDNTFMHWYQQRPGQSPSLIYRASILQ SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCHQSIEDPYTFGGGTKLEIK
1011.	PM26C9-LCDR1	artificial	aa	RASESIDSYDNTFMH
1012.	PM26C9-LCDR2	artificial	aa	RASLQS
1013.	PM26C9-LCDR3	artificial	aa	HQSIEDPYT
1014.	PM26C9-L	artificial	nt	GACGTGCTGATGACCCAGTCTCCACTCTCCCTGGCTGTGACTCTGGGCCAGCCGG CCTCCATCTCTTGGCGGCCCTCCGAGTCCATCGACTCCGACACACACCTTTCATG CACTGGTATCAGCAGAGGCCCTGCCAGTCTCTAGCCTGCTGATCTACCGGGCCT CTATCCTGCAATCCGGCGTCCCTGACCGGTTCTCCGGCTCTGGCTCCGGTACCGA

55	1015.	PM26C9-LH	artificial	aa	<p>CTTCACCTGAAAATCTCCGCTGTGGAGGCCGAGGACGTGGCGGTCTACTACTGC CACCAGTCCATCGAGGACCCCTACACCTTCGGCGGAGGACCAAGCTGAAATCA AG</p> <p>DVMTQSPSLAVTLGQPASISCRASEIDSNDTFMHWYQQRPGQSPSLIYRASILQ SGVPDRFSGSGTDFTLKISRVEAEDVGYVYCHQSIEDPYTFGGTKLEIKGGGSG GGSGGGGSQLVQSGPEVKPGASVKVSKASGYTFTGYVMHWVRQTPGQRLE WIGYINPYNDVTRYNGKFKGRVTITSDKSSSTAYMELSSLRSEDTAVYYCARGENWYF DSWGRGLVTVSS</p>
50	1016.	PM26C9-LH	artificial	nt	<p>GACGTCGTGATGACCCAGTCTCCACTCTCCCTGGCTGTGACTCTGGGCCAGCCGG CCTCCATCTCTTGGCGGGCTCCGAGTCCATCGACTCCTACGACACACCTTTCATG CACTGGTATCAGCAGAGGCTGGCCAGTCTCCTAGCCTGCTGATCTACCGGCCCT CTATCCTGCAATCCGGCTCCCTGACCGGTTCTCCGGCTCTGGCTCCGGTACCGA CTTCACCTGAAAATCTCCGCTGTGGAGGCCGAGGACGTGGCGGTCTACTACTGC CACCAGTCCATCGAGGACCCCTTACACCTTCGGCGGAGGACCAAGCTGAAATCA AGGTCGTGCTGCTTCTGGCGGCGGCTCCGCTCGGTCGTGCTTCTCAGGTGC AGCTGGTCCAGTCCGGCCCTGAGGTGGTGAAGCCTGGCGCCTCCGTGAAGGTGTC CTGCAAGGCCTCCGGCTACACCTTACCAGGCTACGTGATGCACTGGTGAGACAG ACACCGGCCAGCGGCTGGAATGGATCGGCTACATCAACCTTACACGACGCTGA CCCGGTACAACGGCAAGTTCAAGGGCAGAGTACCATACCAGCGACAAGTCCCTCC TCCACCGCTACATGAACTGTCCAGCCTGAGGCTGAGGCTGAGGACACCGCGTGTACTA CTGCGCCAGGGCGGAGAACTGGTACTACTTCCGACTCTCTGGGCGAGAGGCACTCTG GTCACCGTCTCCTCC</p>
45	1017.	PM26C9 LH X I2C HL	artificial	aa	<p>DVMTQSPSLAVTLGQPASISCRASEIDSNDTFMHWYQQRPGQSPSLIYRASILQ SGVPDRFSGSGTDFTLKISRVEAEDVGYVYCHQSIEDPYTFGGTKLEIKGGGSG GGSGGGGSQLVQSGPEVKPGASVKVSKASGYTFTGYVMHWVRQTPGQRLE WIGYINPYNDVTRYNGKFKGRVTITSDKSSSTAYMELSSLRSEDTAVYYCARGENWYF DSWGRGLVTVSSGGGGSEVLVESGGGLVQPGGSLKSCAASGFTFNKYAMNWR QAPGKLEWARIKSYNNYATYADSVKDRFTISRDDSKNTAYLQMNLIKTEDTAVY YCVRHGNFNSYISWAYWGQGLTVSSGGGGGGGGGGGSGTQVVTQEPSTV SPGGTVTLTCSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTPARFSGSLL GGKAALTLSGVQPEDEAEYCVLWYSNRWVFGGTKLTVL</p>
55	1018.	PM26C9 LH X I2C HL	artificial	nt	<p>GACGTCGTGATGACCCAGTCTCCACTCTCCCTGGCTGTGACTCTGGGCCAGCCGG CCTCCATCTCTTGGCGGGCTCCGAGTCCATCGACTCCTACGACACACCTTTCATG CACTGGTATCAGCAGAGGCTGGCCAGTCTCCTAGCCTGCTGATCTACCGGCCCT CTATCCTGCAATCCGGCTCCCTGACCGGTTCTCCGGCTCTGGCTCCGGTACCGA CTTCACCTGAAAATCTCCCGTGTGGAGGCCGAGGACGTGGCGGTCTACTACTGC</p>

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1025.	PM26H4-LCDR1	artificial	aa	SGVPARFSGSGGTDFTLAISRVEAEDVGVYCHQSIEDPYTFGGGKLEIK
1026.	PM26H4-LCDR2	artificial	aa	RASEIDSYGNTFMH
1027.	PM26H4-LCDR3	artificial	aa	RASILES
1028.	PM26H4-L	artificial	nt	HQSIEDPYT GACGTCGTGATGACCCAGTCTCCACTCTCCCTGGCTGGCTGTGACTCTGGGCCAGCGGG CCTCCATCTCTTCCGGGCTCCGAGTCCATCGACTCCTACGGCAACACCTTCATG CACTGGTATCAGCAGAGGCTGGCCAGTCTCCTCGCTGCTGATCTACCGGCCCT CTATCCTGGAATCCGGGCTCCCTGCCGGTTCTCCGGCTCTGGCTCCGGCACCGA CTTACCCCTGGCAATCTCCCGTGTGGAGGCCGAGGACGTGGCGTCTACTACTGC CACCAGTCCATCGAGGACCCTTACACCTTCGGCGGAGGACCAAGCTGGAATCA AG
1029.	PM26H4-LH	artificial	aa	DVVMTQSPLSLAVTLQQRASISCRASEIDSYGNTFMHVYQRPQSPRLLIYRASILE SGVPARFSGSGGTDFTLAISRVEAEDVGVYCHQSIEDPYTFGGGKLEIKGGGSG GGSGGGGSGVQLVQSGPEVKPGASVKVSKASGYFTGYLHWVKQTPGQRLEW IGYINPYNDVTRYNGKFGRVTITSDTSASTAYMELSGLTSEDATVYVCARGENWYYFD SWGRGLTVTVSS
1030.	PM26H4-LH	artificial	nt	GACGTCGTGATGACCCAGTCTCCACTCTCCCTGGCTGGCTGTGACTCTGGGCCAGCGGG CCTCCATCTCTTCCGGGCTCCGAGTCCATCGACTCCTACGGCAACACCTTCATG CACTGGTATCAGCAGAGGCTGGCCAGTCTCCTCGCTGCTGATCTACCGGCCCT CTATCCTGGAATCCGGGCTCCCTGCCGGTTCTCCGGCTCTGGCTCCGGCACCGA CTTCACCCCTGGCAATCTCCCGTGTGGAGGCCGAGGACGTGGCGTCTACTACTGC CACCAGTCCATCGAGGACCCCTTACACCTTCGGCGGAGGACCAAGCTGGAATCA AGGTGGTGGTGTCTGGCGCGCGGCTCCGGTGGTGGTGTCTCAGGTGC AGTGGTCCAGTCCGGCTGAGGTGGTGAAGCTGGCGCTCCGTGAAGGTGC CTGAAGGCTCCGGCTACACCTCACCGGCTACGTGCTGCACTGGTGAAACAG ACACCGGCCAGCGGCTGGAATGGATCGGTACATCAACCTTACAACGACGTGA CCGGGTACAACGGCAAGTTCAAGGCGAGTCAACCATACAGCGACACGTCCCG CTCCACCGCTACATGGAAGTGTCCGGCTGACGTCTGAGGACACCGCGCTGATT ACTGCGCCAGGCGGAGAACTGGTACTACTTCGACTCTCTGGGCGAGAGGCACTCT GGTACCGTCTCCTCC
1031.	PM26H4 LH X I2C HL	artificial	aa	DVVMTQSPLSLAVTLQQRASISCRASEIDSYGNTFMHVYQRPQSPRLLIYRASILE SGVPARFSGSGGTDFTLAISRVEAEDVGVYCHQSIEDPYTFGGGKLEIKGGGSG GGSGGGGSGVQLVQSGPEVKPGASVKVSKASGYFTGYLHWVKQTPGQRLEW IGYINPYNDVTRYNGKFGRVTITSDTSASTAYMELSGLTSEDATVYVCARGENWYYFD SWGRGLTVTVSSGGGSEVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVR QAPGKGI EWARIISKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNLLKTEDTAVY

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5	CAAATTCATCTCAGTGGAAAGAGTTTGGCCTGGACTCTGTTGAGCTGGCACATTAT GACGTCCTGTTGCTTACCCAAATAAACTCATCCCAATTACATCTCAATCATTAATG AAGACGGAAATGAGATCTTCAAACATCATTAGCTGAAGTGCACCCCGGGATATG AGAACATATCAGATGATGTCACCATACAGTGCCTTCTCTCCACAAGGGACACCC GAGGGGACCTAGTGTATGTGAACATATGCACGGACTGAAGACTTTTTAAATTGGA GCGGACATGAAGATCAATTGCTCCGGGAAATTTGTATTGCCAGATACGGGAAAG TTTTAGAGGAAATAAGTTAAATGCTCAGCTGGCAGGCGCCAAAGGAGTGATTCT TCTACTGACCTGCTGATTACTTTGCTCCCGGGTGAAGTCATATCCAGATGGCT GGAATCTTCCCGAGGTGGTGTGACGCGTGGAAACATCCTAAATCTCAATGTTGCA GGGACCTCTCACCCAGGTACCCCGCAATGAATACGCTTATAGGGGGGAAT TGCAGAAGCTGTTGGTCTGCCAAGTATCCAGTTCATCCAATCGGATACATGACGC ACAGAAGCTGCTAGAAAAGATGGTGGTCCGCACCAACAGACAGCAGCTGGAGG GGAAGTCTCAAGGTGCCCTACAACGTTGGACCTGGATTTACTGGAAATTTTTCTACA CAGAAAGTCAAAATGCACATCCATTCTACCAATGAGGTGACAAGAATCTACAATGTG ATCGGTACTCTCAGGGAGCAGTGGAGCCAGACAGGTATGTCATTCTCGGAGGTC ACCGGACTCATGGGCTTTTGGTGTATCGACCTCAGAGCGGAGCAGCTGTGGT TCATGAAATCGTGAGGAGCTTCGGAACACTGAAGAAGGAGGCTGGAGACCTAGG AGACAATCTTGTGCAAGTTGGGATGCAGAGGAATTTGGTCTGCTGGTTCTACC GAGTGGCAGAAAGAACTCAAGACTCCTGCAAGAGCGTGGAGTGGCTTATATCAA TGCTGACTCCTCTATAGAAAGGCAACTACACCTGAGAGTTGACTGTACACCCCTGAT GTACAGTTTGGTACACAACTTAACAAAAGAACTGAAAAGCCCGATGAAGGCTTCGA AGGCAAAATCCCTTTATGAAAGCTGGACTAAAAGAGTCCCTCCCTGAGTTCAGTGG AATGCCAGGATCAGCAAAATGGGCTCTGGAATGACTTTGAGGTGTTTTTCCAACG ACTGGAAATGCTTCCGGCAGAGCACGCTATATACTAAAACCTGGAAACAAATAAATT CAGTGGCTATCCCTGTATCACAGCGTCTATGAAACCTATGAGTTGTCGAAAAGTT TTACGATCCAAATGTTCAAAATACACCTGACTGTGGCTCAGGTTGAGGCGGGATGG TGTTGAGCTAGCCAACTCCATAGTGTGCTGCTTTTATTGCCGAGATTATGCCGTAG TTTTAAGGAAGTATGCTGATAAAATCTACAGCATTTCTATGAAGCATCCACAGGAGA TGAAGACATATAGTGATCATTCGATTCACTTTCTCTGCAGTGAAGAATTTTACCGA AATTGCTTCTAAGTTTAGTGAGAGGCTCCAGGACTTCGACAAAAGCAATCCAATAGT ATTGAGAAATGATGAACGATCAACTGATGTTTCTGGAGAGAGCATTTATCGATCCATT AGGCTTACCAGACCGCCCTTTTATAGACATGTCATCTACGCTCCAAGCAGTCACAA CAAGTACGCAGGGAGTCTTCCAGGAATCTATGCCCCTGTTTGACATTGAAA GCAAGGTGGACCTTCTAAGGCTGGGCGAAGTGAAGAGGCAGATTATGTGGC AGCCTTCAACCGTGACGCGCAGACGCTTGAAGGTAGGCTCCCGGGAT TACAAGGACGACGATGACAAGTAA
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1034.	huPSMArat140- 169	artificial	aa	<p>MWNLHETDSAVATARRPRWLCAGALVLAGGFFLLGLFLGWFIKSSNEATNTPKHNM KAFDELKAENIKFLYNFTQIPLHAGTEQNFQAKIQSQWKFEGLDSVELAHYDVLLS YPNKTHPNYSIINEDGNEIFKTSIAELSPPGYENISDVPPYSAFSPQGTPEGDLVYVNY ARTEDFFKLERDMKINCSGKIVARYGKVFGRGNVKNQAQAGKGVLYSDPADYFAPG VKSYPDGWNLPGGGVQRGNILNLNGAGDPLTPGYPANAYRRGIAEAVGLPSIPVHP GYDDAQKLEKMGSSAPPDSSWRGSLKVPYNVGPFTGNFSTQKVKMHIHSTNEVTRI YNVIGTLRGAVEPDYVILGGHRDSWVFGIDPQSGAAVHVEIRSFGLKKEGWRPR RTILFASWDAEEFGLLGSTEWAEENSRLQERGVAYINADSSIEGNYTLRVDCPTLMYS LVHNLTKELKSPDEGFEKSLYESWTKKSPSEFSGMPRISKLGSGNDFEVFFQRLGIA SGRARYTKNWETNKFSGYPLYHSVYETVELVEKFYDPMFKYHLTVAQVRGGMVFELA NSIVLPFDCRDYAVLRYADKIYSISMKHPQEMKTSVSFDSLSFSAVKNFTEIAKFSFSE RLQDFDKSNPIVLRMMNDQLMFLERAFIDPLGLPDRPFYRHVIYAPSSHKNKYAGESFPFGI YDALFDIESKVDPSKAWGEVKRQIYVAFTVQAAETLSEVASGDYKDDDDK</p>
1035.	huPSMArat191- 258	artificial	nt	<p>ATGTGGAATCTGCTTCACGAAACAGACTCGGCTGTCCACCGCGCGCGCGCGC GGTGGCTGTGCGCGCGCGGCTGGTCTCTGGCGGTGGATTCTTCTCTGGGCTT CCTCTTTGGGTGTTTATCAATCCTCAACGAAGCTACTAATATTACTCCAAAACAT AATATGAAGGCATTTTGGACGAATTGAAAGCCGAGAACATCAAAAAGTTCTTATAC AATTTACCCAGATACCACACTTAGCAGGAAACCAACAACTCCAGCTTGCAAAA CAAAATCAATCTCAGTGAAAGAGTTTGGCTGGACTCTGTTGAGCTGGCACATTAT GACGCTCTGTTGCTTACCCAAATAAACTCATCCCAATTACATCTCAATCATTAATG AAGACGGAATGAGATCTTCAACACATCCTTATTTGAACCCCTCTCCAGGCTATG AAAATGTGTCGGATATTGTGCCACCTTTCAGCGCTTCTCTCCCAAGGAATGCCCG AGGGCGACCTAGTGTATGTGAACCTATGCGGCACCTGAAGACTTTTAAATGGAG CGGGTCATGAAGATCAATTGTTCTGGGAAGATTGTATCGCCAGATATGGCCAAGT GTTCAAGAGGAAACAAGGTTAAAAACGCTCAGCTGGCAGGTGCAAAAGGAATCATTC TGACTCAGACCCCTGCTGATTACTTTGTTCTGGCGTGAAGTCTACCCAGATGGCT GGAACCTCCCTGGAGGTGGCGTTCAGCGTGAAACGTCCTAACTCAATGGTGCA GGCAGCCCGTTAACCCAGGTTACCCCGCAATGAATACGCTTAGCGCGGGAAT TGCAGAAGCTGTTGGTCTGCCAAGTATCCAGTTCATCCAATCGGATACATGACGC ACAGAAGCTGCTAGAAAAGATGGTGGCTCCGCACCAACAGACAGCAGCTGGAGG GGAAGCTTGAAGGTGCCCTACAACGTTGGACCTGGATTACTGGAATTTTCTTACA CAGAAAGTCAAAATGCACATCCATTCTACCAATGAGGTGACAAGAACTACAATGTG ATCGGTACTCTCAGGGAGCAGTGGAGCCAGACAGGTATGTCTCTCGGAGGTC ACCGGACTCATGGGTCTTTGGTGGTATCGACCCCTCAGACGGGAGCGAGCTGGT TCATGAAATCGTGAGGAGCTTCGGAACACTGAAGAAGGAAGGCTGGAGACCTAGG AGAACAACTTGTGCAAGTTGGGATGCAGAGGAATTTGGTCTGCTTGGTCTTAC</p>

<p>GAGTGGCAGAGAACTCAAGACTCCTGCAAGAGCGTGGAGTGGCTTATATCAA TGCTGACTCCTCTATAGAAAGCAACTACACCTGAGAGTTGACTGTACACCCCTGAT GTACAGTTTGGTACACAATCTAACAAAGAACTGAAAGCCCGGAGAGGCTTCGA AGGCAATCCCTTTATGAAAGCTGGACTAAAAGAGTCCCTCCCTGAGTTCAGTGG AATGCCAGGATCAGCAAAATGGCTCTGGAATGACTTGGAGTGTTCCTCAACG ACTGGAAATTCCTCCGGCAGAGCAGCTATACCTATACTAAAACCTGGAAACAAATAAT CAGTGGCTATCCCTGTATCAGCGCTATGAAACCTATGAGTTGGTGAAGAGTT TTACGATCCAATGTTCAAATATCACCTGACTGTGGCTCAGGTTGAGGCGGGATGG TGTCGAGCTAGCCAACTCCATAGTGTGCTGCTTTTATTGCCGAGATTATGCCGTAG TTTTAAGGAAGTATGCTGATAAATCTACAGCAATTTCTATGAAGCATCCACAGGAGA TGAAGACATATAGTGATCATTCGATTCACTTTCTCTGCAGTGAAGAATTTTACCGA AATTGCTCTAAGTTTAGTGAGAGGCTCCAGGACTCGACAAAGCAATCCAATAGT ATTGAGAAATGATGAACGATCAACTGATTTCTGGAGAGAGCATTTATCGATCCATT AGGCTTACCAGACCCCTTTTATAGACATGTCATCTACGCTCCAAGCAGTCACAA CAAGTACGCGAGGGAGTCTTCCAGGAATCTATGATGCCCTGTTGACATTGAAA GCAAGGTGGACCTTCTAAGGCTGGGCGAAGTGAAGAGGAGCATTTATGTGGC AGCCTTACCGTGCAGGCGAGCCGACAGACCTTGAGTGAGGTAGCCTCCGGGGAT TACAAGCAGCAGTACACAAGTAA</p>				<p>1036.</p>
<p>MWNLLHETDSAVATARRPRWLCAGALVLAGGFFLLGLFGWFIKSSNEATNITPKHNM KAFDELKAENIKKFLYNTQIPHLAGEQNFLAKIQSQWKEFGLDVSELAHYDVLLS YPNKTHPNYSIINEDGNEIFNTSLFEPPIPGYENVSINVPFSAFSPQGMPEGDLVYVN YARTEDFFKLERVMKINCSGKIVARYQVFRGNKVNAQLAGAKGILYSDPADYFVPG VKSYPDGNLPGGGVQRGNVLNLNGAGDPLTPGYPANAYAYRRGIAEAVGLPSIPVHP IGYYDAQKLEKMGGSAPPDSSWRGSLKVPYNVPGFTGNFSTQVKMHIHSTNEVTR YNVIGTLRGAVEPDYVILGGHRDSWVFGGIDPQSGAAVWHEINRSFGLKKEGWPRR RTILFASWDAEEFGLLGSTEWAEENSRLQERGVAYINADSSIEGNYTLRVDCITPLMYS LVHNLTKELKSPDEGEGKSLYESWTKKSPSPFSGMPRISKLGSGNDFEVFFQRLGIA SGRARTKNWETNKFSGYPLVHSVYETVELVEKFDPMFYHLTVAQVRGGMVFELA NSIVLPFDCRDYAVLRYADKIYISIMKHPQEMKTSVSFDSLSFAVKNFTEIASKFSE RLQDFDKSNPIVLRMMNDQLMFLERAFIDPLGLPDRPFYRHVYAPSSHNKYAGESFPGI YDALFDIESKVDPSKAWGEVKRQIYVAAFTVQAAETLSEVASGDYKDDDDK</p>	aa	artificial	huPSMArat191- 258	
<p>ATGTGGAATCTGCTTACGAAACAGACTCGGCTGTGCGCACCCGCGCGCCCGC GGTGGCTGTGCGCGCGCGCTGGTCTGCGGGTGGATTCTTCTCCTGGGCTT CCTCTTGGGTGTTATCAAATCCTCAACGAAGCTACTAATACTCCAAACAT AATATGAAGGCATTTTGGACGAATTGAAAGCCGAGAACATCAAAAAGTCTTATAC AATTTTACCCAGATACCACACTTAGCAGGAACCGCAACAACTTCCAGCTTGCAAAA</p>	nt	artificial	huPSMArat281- 284	<p>1037.</p>

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CAAAATCAATCTCAGTGGAAAGAGTTTGGCCTGGACTCTGTTGAGCTGGCACATTAT
GACGTCTGTTGTTACCCAAATAAACTATCCCAATTACATCTCAATCATTAATG
AAGACGGAAATGAGATCTTCAACACATCTTATTTGAACCCCTCTCCAGGCTATG
AAATGTGTGGATATTGTGCCACCTTTCAGCGTTTCTCCCCAAGGAATGCCCG
AGGCGACCTAGTGTATGTGAACATGACCGGACTGAAGACTTTTTAAATGGAGC
GGACATGAAGATCAATTGCTCCGGGAAATTTGATTGCCAGATACGGGAAAGTT
TTAGAGGAAATAAAGTTAAATGCTCAGCTGGCAGCGCCAAAGGAGTGATTCT
CTACTCTGACCTGCTGATTACTTTGCTCCCGGGTGAAGTCATATCCAGATGGCT
GGAATCTTCCCGAGGTGGTGTGACGCTGGAACATCCTAAATCTCAATGGTGCA
GGGACCCGTTAACCCAGGTTACCCCGCAATGAATACGCTTATAGGCATGAGTT
CACAGAAGCTGTTGGTCTGCCAAGTATCCAGTTCATCCAAATCGGATACATGACGC
ACAGAAGCTGCTAGAAAAGATGGTGGCTCCGCACCCACAGACAGCAGCTGGAGG
GGAAGCTTGAAGGTGCCCTACAACGTTGGACCTGGATTACTGGAAATTTTCTACA
CAGAAAGTCAAAATGCACATCCATTCTACCAATGAGGTGACAAGAACTACAAATGTG
ATCGGTACTCTCAGGGGAGCAGTGAGCCAGACCGGTATGTCATTCTCGGAGGTC
ACCGGACTCATGGGCTTTGGTGTATCGACCTCAGAGCGGAGCAGCTGTGGT
TCATGAAATCGTGAGGAGCTTCGGAACACTGAAGAGGAATTTGGTCTGTTGGTCTACC
AGAACAATCTTGTGCAAGTTGGGATGCAGAGGAATTTGGTCTGTTGGTCTTACC
GAGTGGCAGAGAGAACTCAAGACTCTCGCAAGAGCTGGAGTGGCTTATATCAA
TGCTGACTCCTCTATAGAAGGCAACTACACCTGAGAGTTGACTGTACACCCCTGAT
GTACAGTTTGTACACAATCTAACAAGAACTGAAAGCCCGGATGAAGGCTTCGA
AGGCAATCCCTTTATGAAAGCTGGACTAAAAGAGTCCCTCCCTGAGTTCAGTGG
AATGCCCAGGATCAGCAAAATGGGCTCTGGAATGACTTTGAGGTGTTTTCCAAAG
ACTGGGAATTGCTCCGGCAGAGCACGCTATACATAAACTGGGAACAAATAAAT
CAGTGGCTATCCCTGTATCACAGCGTCTATGAAACCTATGAGTTGTCGAAAGTT
TTACGATCCAATGTTCAAATATCACCTGACTGTGGCTCAGGTTGAGCGGGATGG
TGTTGAGCTAGCCAACTCCATAGTGTGCTGCTTTTATGATGCCGAGATTATGCCGTAG
TTTTAAGGAAGTATGCTATAAATCTACAGCATTTCTATGAAGCATCCACAGGAGA
TGAAGACATATAGTGTATCATTCGATTCACTTTTCTCTGCAGTGAAGAAATTTACCGA
AATTGCTTCTAAGTTTAGTGAGAGGCTCCAGGACTTCGACAAAAGCAATCCAATAGT
ATTGAGAATGATGAACGATCAACTGATGTTCTGGAGAGAGCATTTATCGATCCATT
AGGCTTACCAGACCGCCCTTTTATAGACATGTCATCTACGCTCCAAAGCAGTCACAA
CAAGTACGCGAGGGAGTCTTCCAGGAATCTATGATGCCCTGTTTGACATTGAAA
GCAAGGTGGACCTTCTAAGGCTGGGCGAAGTGAAGAGGCAGATTATGTGGC
AGCCTTCAACCGTGCAAGCGCCGACAGACCTTGAGTGAGGTAGCCTCCGGGGAT
TACAAGGACGACGATGACAAGTAA

1038.	huPSMArat281- 284	artificial	aa	<p>MWNLLHETDSAVATARRPRWL CAGALVLAGGFLLGLFGWFIKSSNEATNITPKHNM KAFDELKAENIKFLYNFTQIPHLAGTEQNFQLAKIQISQWKEFGLDSELAHYDVLLS YPNKTHPNYISIINEDGNEIFNTSLFEPPPPGENYVSDIVPPSFAFSPQGMPEGDLVYVN YARTEDFFKLERDMKINCSGKVIARYGKVFGRGNKVKNAAGAKGVILYSDPADYFAP GVKSYPDGWNLPGGVQQRGNILNLNGAGDPLTPGYPANHEYARHEFTEAVGLPSIPVH PIGYDAQKLLKMGSGAPPDSSWRGSLKVPYNVGPFTGNFSTQVKMHIHSTNEVT RIYNVIGTLRGAVEPDYVILGGHRDSWVFGIDPQSGAAVWHEIVRSFGLKKEGWRP RRTILFASWDAEEFGLLGSTEWAEENSRLQERGVAYINADSSIEGNYTLRVDCTPLMY SLVHNLTKELKSPDEGFEKSLYESWTKKSPSPFSGMPRIKLSGNDFEVFFQRLGI ASGRARYTKNWETNKFSGYPLYHSVYETVELVEKFYDPMFKYHLTVAQVRGGMVFELA NSIVLPFDCRDYAVLRYADKIYSISMKHPQEMKTVSVFDSLFSAVKNFTEIAKFSFSE RLQDFDKSNPIVLRMMNDQLMFLERAFIDPLGLPDRPFYRHVIYAPSSHNKYAGESFPFGI YDALFDIESKVDPSKAWGEVKRQYVAAFTVQAAETLSEVASGDYKDDDDK</p> <p>ATGTGGAATCTGCTTCACGAAACAGACTCGGCTGTGCGCACCGCGCGCGCCCGC GGTGGCTGTGCGCGGGCGCTGGTCTGCGGGTGGATTCTTCTCTGGGCTT CCTCTTGGGTGGTTATCAAACTCTCAACGAAGCTACTAATAATTACTCCAAACAT AATATGAAGGCATTTTGGACGAATTGAAAGCCGAGAACATCAAAAAGTTCTTATAC AATTTTACCCAGATACCCACACTTAGCAGGAGCCGAAACAACTCCAGCTTGCAAAA CAAAATCAATCTCAGTGGAAAGAGTTGGCTGGACTCTGTTGAGCTGGCACATTAT GACGTCTCTGTTGCTTACCCAAATAAACTCATCCCAATTACATCTCAATCATTAATG AAGACGGAAATGAGATCTTCAACACATCCTTATTTGAACCCCTCTCCAGGCTATG AAATGTGTGGATATTGTGCCACCTTTCAGCGCTTCTCTCCCAAGGAATGCCCG AGGGCGACCTAGTGTATGTGAACATATGCACGGACTGAAGACTTTTTTAAATTGGAGC GGGACATGAAGATCAATTGCTCCGGGAAATTTGATTGCCAGATACGGGAAAGTT TTTAGAGGAAATAAAGTTAAATGCTCAGCTGGCAGGCGCAAGGAGTGATTCT CTACTCTGACCTGCTGATTACTTTGCTCCGGGTGAAGTCATATCCAGATGGCT GGAATCTTCCCGAGGTGGTGCAGCGTGGAAACATCCTAAATCTCAATGGTGCA GGCGACCCGTAAACCCAGGTTACCCCGCAAATGAATACGCTTATAGCGGGGAAT TGCAGAAAGCTGTGGTCTGCCAAGTATCCAGTTATCCCAATCGGATACGATGATGC CCAGAAACTATTAGAACATATGGTGGCTCCGACCCCTGACAGCAGCTGGAAGG GAGGACTAAAAGTGCCTTACAACGTGGGACCTGGCTCGCTGGAACCTTCTCAAAA CAAAAGGTCAAGCTGCACATCCATTCTACCAATGAGGTGACAAAGATCTACAATGTG ATCGGTACTCTCAGGGGAGCAGTGGAGCCAGACCGGTATGTCAATCTCGGAGGTC ACCGGACTCATGGGTCTTTGGTGGTATCGACCCCTCAGAGGAGCAGCTGTGGT TCATGAAATCGTGAGGAGCTTCGGAACACTGAAGAAGGCTGAGACCTTAGG AGAACAACTTGTGTTGCAAGTTGGGATGCAGAGGAATTTGGTCTGCTTGGTTCTACC</p>
1039.	huPSMArat300- 344	artificial	nt	

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				GAGTGGCAGAGAGAACTCAAGACTCCTGCAAGAGCGGTGAGTGGCTTATATCAA TGCTGACTCCTCTATAGAAGGCAACTACACCTGAGAGTTGACTGACACCCCTGAT GTACAGTTTGGTACACAATCTAACAAGAACTGAAAGCCCGATGAAGGCTTCGA AGGCAATCCCTTTATGAAGCTGGACTAAAAGAGTCTTCCCTGAGTTCAGTGG AATGCCAGGATCAGCAATGGGCTCTGGAATGACTTGGAGTGTTCCTTCCAAACG ACTGGGAATTGCTTCGGCAGAGCAGCTATCTAATAAAGTGGAAACAAATAAAT CAGTGGCTATCCCTGTATCACAGCGTCTATGAACCTATGAGTTGGTGAAGAGTT TTACGATCCAATGTTCAAATATACCTGACTGTGGCTCAGTTTCGAGCGGGATGG TGTTGAGCTAGCCAACTCCATAGTGTGCTGCTTTGATGCCGAGATTATGCCGTAG TTTTAAGGAAGTATGCTGATAAAATCTACAGCATTTCTATGAAGCATCCACAGGAGA TGAAGACATATAGTATCATTCGATTCACTTTCTCTGCGATGAAGAATTTTACCGA AATTGCTTCTAAGTTAGTGAGAGGCTCCAGGACTTCGACAAAGCAATCCAATAGT ATTGAGAATGATGAACGATCAACTGATGTTCTGAGAGAGCATTTATCGATCCATT AGGCTTACCAGACGCGCTTTTATAGACATGTCATCTACGCTCCAAGCAGTCACAA CAAGTAGCGAGGGAGTCTTCCAGGAATCTATGATGCCCTGTTGACATTGAAA GCAAGGTGGACCTTCTAAGGCTGGGCGAAGTGAAGAGCGAGATTATGTGGC AGCCTTCAACCGTGACGCGCGCAGAGACCTTGAGTGAGGTAGCCTCCGGGGAT TACAAGGACGACGATGACAAAGTAA
1040.	huPSMArat300- 344	artificial	aa	MWNLHETDSAVATARPRWLCAALVLAGFFLLGFLGWFHFKSSNEATNTPKHNH KAFDELKAENIKKFLYNFTQIPHLAGTEQNFQAKQIQSQWKEGLDSVELAHYDVLLS YPNKTHPNYISIINEDGNEIFNTSLFEPPIPGYENVSIVPFSFSPQGMPEGDLVYVN YARTEDFFKLERDMKINCSGKIVARYGKVRGNKVKNAQLAGAKGVILYSDPADYFAP GVKSYPDGWNLPGGGVQRGNILNLNGAGDPLTPGYPANAYRRIAGAEAVGLPSIPVH PIGYDDAQKLLHMGSAAPPDSSWKGLKVYNVPGFAGNFSKQVKLHIHSTNEVT RIYNVIGTLRGAVEPDYVILGGHRDSWVFGGIDPQSGAAVHEIVRSFGTLKKEGWRP RRTILFASWDAEEFGLLSTEWAEENSRLQERGVAYINADSSIEGNYTLRVDCTPLMY SLVHNLTKELKSPDEGFEGKSLYESWTKSPSPFSGMPRISKLGSNDFEVFFQRLGI ASGRARYTKNWETNKFSGYPLYHSVYETELVEKFYDPMFKYHLTVAQVRGGMVFELA NSIVLPFDCRDYAVVLRKYADKIYSISMKHPQEMKTSVSFDSLFSVAKNFTEIASKFSE RLQDFDKSNPIVLRMMNDQLMFLERAFIDPLGDPDRPFYRHVIYAPSSHKNKYAGESFPGI YDALFDIESKVDPSKAWGEVKRQIYVAAFTVQAAETLSEVASGDYKDDDDK ATGTGGAATCTGCTTACGAAACAGACTCGGCTGTCCGACCGCGCGCGCGCGCGC GTGGCTGTGGCGCGCGCGCTGCTGCTGGCGGGTGGAATTTCTCTCTCTGGCTT CCTCTTTGGGTGGTTTATCAATCCTCCAACGAAGCTACTAATTTACTCCAAACAT AATATGAAGGCATTTTGGACGAATTGAAAGCCGAGAACATCAAAAAGTTCTTTATAG AATTTACCCAGATACCACTTAGCAGGAACCGGAACAACTTCCAGCTTGCAGAAA
1041.	huPSMArat598- 617	artificial	nt	

5	CAAAATCAATCTCAGTGGAAAGAGTTGGCCTGGACTCTGTTGAGCTGGCACATTAT GACGTCTGTTGCTTACCCAAATAAACTCATCCCAATTACATCTCAATCATTAATG AAGACGGAAATGAGATCTTCAACACATCCTTATTTGAACCCCTCTCCAGGCTATG AAATGTGTCGGATATTGTGCCACCTTTCAGCGCTTCTCTCCCAAGGAATGCCCG AGGCGACCTAGTGTATGTGAACATATGCACGGACTGAAGACTTTTTTAAATTGGAGC GGGACATGAAGATCAATTGCTCCGGGAAATGTGATTGCCAGATACGGGAAAGTT TTTAGAGGAAATAAGTTAAATGCTCAGCTGGCAGCGGCCAAAGGAGTGATTCT CTACTCTGACCTGCTGATTACTTTGCTCCCGGGTGAAGTCATATCCAGATGGCT GGAATCTTCCGGAGTGTGTGCAGCGTGGAAACATCCTAAATCTCAATGTTGCA GGGACCCCTCTACCCAGGTTACCCCGCAATGAATACGCTTATAGGGGGAAAT TGCAGAAAGCTGTTGGTCTGCCAAGTATCCAGTTCATCCAAATCGGATACATGACGC ACAGAAGCTGCTAGAAAAGATGGTGGTCCGCACCCACAGACAGCAGCTGGAGG GGAAGTCTCAAGTGCCCTACAACGTTGGACCTGGATTACTGGAAATTTTCTACA CAGAAAGTCAAAATGCACATCCATTCTACCAATGAGGTGACAAGAACTACAATGTG ATCGGTACTCTCAGGGGAGCAGTGGAGCCAGACAGGTATGTCATCTCGGAGGTC ACCGCGACTCATGGTCTTTGGTGTATCGACCTCAGAGCGGAGCAGCTGTGGT TCATGAAATCGTGAGGAGCTTCGGAACATCGAGAGGAATTTGGTCTGTTGGTCTACC AGAACAATCTTGTGCAAGTTGGGATGCAGAGGAATTTGGTCTGTTGGTCTTACC GAGTGGCAGAAAGAACTCAAGACTCTGCAAGAGCGTGGAGTGGCTTATATCAA TGCTGACTCCTCTATAGAAGGCAACTACACCTGAGAGTTGACTGTACACCCCTGAT GTACAGTTTGTACACAATCTAACAAGAACTGAAAAGCCCCGATGAAGGCTTCGA AGGCAATCCCTTTATGAAAGCTGGACTAAAAGAGTCCCTCCCTGAGTTCAGTGG AATGCCCAGGATCAGCAAAATGGGCTCTGGAATGACTTTGAGGTGTTTTCCAAAG ACTGGGAATTGCTTCCGGCAGAGCACGCTATACTAAAACCTGGGAAACAAATAAAT CAGTGGCTATCCCTGTATCACAGCGTCTATGAAACCTATGAGTTGTCGAAAAGTT TTACGATCCAATGTTCAAATATCACCTGACTGTGGCTCAGGTTGAGCGCGGATGG TGTTGAGCTCGCCAACTCCATAGTGTGCTGCTTTTGAATGCCAAAGTTATGCTGTAG CTCTGAAGAAACATGCTGAGACTATCTACAACATTTCAATGAATCATCCACAGGAGA TGAAGACATATAGTGAAGCTTCGATTCACTTTTCTCTGCAAGTGAAGAAATTTACCGA AATTGCTTCTAAGTTTAGTGAGAGGCTCCAGGACTTCGACAAAAGCAATCCAATAGT ATTGAGAAATGATGAACGATCAACTGATGTTTCTGGAGAGAGCATTTATCGATCCATT AGGCTTACCAGACCGCCCTTTTATAGACATGTCATCTACGCTCCAAAGCAGTCACAA CAAGTACGCGAGGGAGTCTTCCAGGAATCTATGACGCTTGTGTTGACATTGAAA GCAAGGTGGACCTTCTAAGGCTGGGCGAAGTGAAGAGGCAGATTATGTGGC AGCCTTCAACCGTGCAAGGCGCCGAGAGACCTTGAGTGAGGTAGCCTCCGGGGAT TACAAGGACGACGATGACAAGTAA
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1042.	huPSMArat598-617	artificial	aa	<p>MWNLHETDSAVATARRPRWLCAGALVLAGGFLLGLFLGWFIKSSNEATNTPKHNM KAFDELKAENIKKFLYNFTQIPHLAGTEQNFQLAKIQSQWKEFGLDSVELAHYDVLLS YPNKTHPNYISIINEDGNEIFNTSLFEPppPYENVSDIVPPFSFSPQGMPEGDLVYVN YARTEDFFKLERDMKINCSGKIARYGKVFRGNKVNAQLAGAGVILYSDPADYFAP GVKSYPDGWNLPGGVQRGNILNLNGAGDPLTPGYPANERYARRGIAEAVGLPSIPVH PIGYYDAQKLLEKMGSGAPPDSSWRGSLKVPYNVGPFTGNFSTQVKMHIHSTNEVT RIYNVIGTLRGAVEPDYVILGGHRDSWVFGGIDPPQSGAAVHEIVRSFGTLKKEGWRP RRTILFASWDAAEEFGLLGSTEWAEENSRLQERGVAYINADSSIEGNYTLRVDCITPLMY SLVHNLTKELKSPDEGFEGKSLYESWTKKSPSPFSGMPRISKLGSGNDFEVFFQRLGI ASGRARYTKNWETNKFSGYPLYHSHVYETVELVEKFDPMFKYHLTVAQVRGGMVFELA NSIVLPFDCQSYAVALKKHAETIYNISMNHPQEMKTVSVFDSLFSVAVKNFTEIAKFSFSE RLQDFDKSNPIVLRMMNDQLMFLERAFIDPLGLPDRPFYRHVIYAPSSHNKYAGESFPGI YDALFDIESKVDPSKAWGEVKRQIYVAAFTVQAAAEITLSEVASGDYKDDDDK</p>
1043.	huPSMArat683-690	artificial	nt	<p>ATGTGGAACTCTGCTTACGAAACAGACTCGGCTGTGCCACCGCGCGCGCGCGC GGTGGCTGTGCGCGCGCGCGCTGGTCTCTGGCGGTGGATTCTTCTCTCGGCTT CCTCTTTGGGTGGTTATCAAACTCTCAACGAGACTATAATTACTCCAAACAT AATATGAAGGCATTTTGGACGAATTGAAAGCCGAGAACATCAAAAAGTCTTTATAC AATTTTACCCAGATACCACACTTAGCAGGAACCGAACAACTTCCAGCTTGCAAAA CAAATTCAACTCAGTGAAAGAGTTGGCTGGACTCTGTGAGCTGGCACATTAT GACGTCCTGTTGCTTACCCAAATAAAACTCATCCCAATTACATCTCAATCATTAATG AAGACGGAAATGAGATCTTCAACACATCTTATTTGAACCCCTCTCCAGGCTATG AAAATGTGCGGATATTGTGCCACCTTTACGCGCTTTCTCTCCCAAGGAATGCCCG AGGGCGACCTAGTGATGTGAACATATGCACGACTGAAGACTTTTTTAAATTGGAGC GGGACATGAAGATCAATTGCTCCGGGAAAATTGTGATTGCCAGATACGGGAAAGTT TTTAGAGGAAATAAGTTAAAATGCTCAGCTGGCAGGCGCCAAAGGAGTGATTCT CTACTCTGACCCCTGCTGATTACTTTGCTCCCGGGTGAAGTCATATCCAGATGGCT GGAATCTTCCCGGAGGTGGTGTGACGCTGGAACATCTCAATCTCAATGGTGCA GGCACCCCTCTCACCCAGGTTACCCCGCAAATGAATACGCTTATAGCGGGGAAT TGCAGAGCTGTGGTCTGCCAAGTATCCAGTTTCAATCCAAATCGGATCTATGACGC ACAGAAAGCTGTAGAAAAGATGGGTGGTCCGACACACAGACAGCAGCTGGAGG GGAAGTCTCAAGGTGCCCTACACGTTGGAACTGGATTACTGGAAATTTTCTACA CAGAAAGTCAAAATGCACATCCATTCTACCAATGAGGTGACAAAGATCTACAATGTG ATCGGTACTCTCAGGGGAGCAGTGGAGCCAGACAGGTATGTCTATCTCGGAGTCTC ACCGGACTCATGGGCTTTGGTGGTATCGACCCCTCAGAGCGGAGCAGCTGTGGT</p>

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1044.	huPSMArat683-690	artificial	aa		<p>MWNLLHETDSAVATARPRWLACAGALVLAGGFFLLGFLFGWFIKSSNEATNITPKHNM KAFDELKAENIKFLYNFTQIPHLAGTEQNFQLAKQIQSQWKEFGLDSVELAHYDVLLS YPNKTHPNYISIINEDGNEIFNTSLFEPPPGYENVSIVPPFSAFSPQGMPEGDLVYN YARTEDFFKLERDMKINCSGKIVARIYKVFGRGNKVKNAQLAGAKGVILYSDPADYFAP GVKSYPDGWNLPGGGVQRGNILNLNGAGDPLTPGYPANAYYRRGIAEAVGLPSIPVH PIGYDDAQKLLKMGGSAPPDSSWRGSLKVPYNVGPFTGNFSTQVK/MHIHSTNEVT RIYNVIGTLRGAVEPDYVILGGHRDSWVFGGIDPQSGAAVWHEIVRSFGLKKEGWPR RRTILFASWDAEEFGLLGSTEWAEENSRLQERGVAYINADSSIEGNYTLRVDCITPLMY SLVHNLTKELKSPDEGFEGKSLYESWTKSPSPFSGMPRISKLGSNDFFVFFQRLGI ASGRARYTKNWETNKFSGYPLYHSVYETVELVEKFDPMFKYHLTVAQVRGGMVFEA NSIVLPFDCRDYAWLIRKYADKIYISIMKHPQEMKTYSVSFDLSFAVKNFTEIASKFSE RLQDFDKSNPIVLRMMNDQLMFLERAFIDPLGPRPFYRHHIYAPSSHNKYAGESFPGI YDALFDIESKVDPKAWGEVKRQIYVAAFTVQAAAETLSEVASGDYKDDDDK</p>
1045.	huPSMArat716-	artificial	nt		ATGTGGAATCTGCTTCACGAAACAGACTCGGCTGTCCGCCACCGCGCGGCCCGC

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1046.	huPSMArat716-750	artificial	aa	<p>CAAGTACGAGGGAGTGCTCCAGGAATCTATGACGCGTGTGACATTAAATAA CAAAGTCGATACTTCTAAGGCCTGGAGAGAGTGAAGACAGATTTCTATTGCAGC CTTTACAGTGAAGCTGCAGCAGAGACTCTGAGAGAAAGTAGACTCCGGGGATTACA AGGACGACGATGACAAGTAA</p> <p>MWNLHETDSAVATARRPRWLCAALVLAGGFLLGFLFGWFIKSSNEATNITPKHNM KAFDELKAENIKKFLYNFTQIPLHAGTEQNFLAKQIQSQWKEFLDSVELAHYDVLLS YPNKTHPNYISIINEDGNEIFNTSLFEPGPPGYENVSDIVPFSFSPQGMPEGDLVYN YARTEDFFKLERDMKINCSGKVIARYGKVFRGNKVKNAQLAGAKGVILYSDPADYFAP GVKSYPDGWNLPGGGVQRGNILNLNGAGDPLTPGYPANERYARRGIAEAVGLPSIPVH PIGYDAQKLLKMGGSAPPDSSWRGSLKVPYNVGPFTGNFSTQVKVMIHSTNEVT RIYNVIGTLRGAVEPDYVILGGHRDSWVFGIDPQSGAAVWHEIVRSFGLKKEGW RP RRTILFASWDAAEEFGLLGSTEWAEENSRLQERGVAYINADSSIEGNYTLRVDC TPLMY SLVHNLTKELKSPDEGFEGKSLYESWTKKSPSPSEFSGMPRISKLGSGNDFEVFFQRLGI ASGRARYTKINWETNKFSGYPLYHSVYETVELVEKFYDPMFKYHLTVAQVRGGMVFELA NSIVLPFDCRDYAVWLRYADKIY SISMKHPQEMKTYSVSFDLSFSAVKNFTEIASKFSE RLQDFDKSNPIVLRMMNDQLMFLERAFIDPLGLPDRPFYRHVIYAPSSHNNKYAGESFPGI YDALFDINNKVDTSKAWREVKRQISIAAFTVQAAAE TLREVDSGDYKDDDDK</p> <p>QDGNEMGSITQTPYQVVISGTTILTC</p>
1047.	Macaca fascicularis CD3ε 1-27	Macaca fascicularis	aa	
1048.	Macaca fascicularis CD3ε 1-27	Macaca fascicularis	aa	QDGNEMGSITQTPYQVVISGTTVILT
1049.	Macaca mulatta CD3ε 1-27	Macaca mulatta	aa	QDGNEMGSITQTPYHVISGTTVILT

[0365] The present invention also relates to the following items:

1. A bispecific single chain antibody molecule comprising a first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 ϵ (epsilon) chain, wherein the epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID NOs. 2, 4, 6, and 8, and a second binding domain capable of binding to prostate-specific membrane antigen (PSMA).

2. The bispecific single chain antibody molecule of item 1, wherein at least one of said first or second binding domain is CDR-grafted, humanized or human.

3. The bispecific single chain antibody molecule according to any one of items 1 or 2, wherein the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 ϵ chain comprises a VL region comprising CDR-L1, CDR-L2 and CDR-L3 selected from:

(a) CDR-L1 as depicted in SEQ ID NO. 27, CDR-L2 as depicted in SEQ ID NO. 28 and CDR-L3 as depicted in SEQ ID NO. 29;

(b) CDR-L1 as depicted in SEQ ID NO. 117, CDR-L2 as depicted in SEQ ID NO. 118 and CDR-L3 as depicted in SEQ ID NO. 119; and

(c) CDR-L1 as depicted in SEQ ID NO. 153, CDR-L2 as depicted in SEQ ID NO. 154 and CDR-L3 as depicted in SEQ ID NO. 155.

4. The bispecific single chain antibody molecule according to any one of items 1 or 2, wherein the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 ϵ chain comprises a VH region comprising CDR-H 1, CDR-H2 and CDR-H3 selected from:

(a) CDR-H1 as depicted in SEQ ID NO. 12, CDR-H2 as depicted in SEQ ID NO. 13 and CDR-H3 as depicted in SEQ ID NO. 14;

(b) CDR-H1 as depicted in SEQ ID NO. 30, CDR-H2 as depicted in SEQ ID NO. 31 and CDR-H3 as depicted in SEQ ID NO. 32;

(c) CDR-H1 as depicted in SEQ ID NO. 48, CDR-H2 as depicted in SEQ ID NO. 49 and CDR-H3 as depicted in SEQ ID NO. 50;

(d) CDR-H1 as depicted in SEQ ID NO. 66, CDR-H2 as depicted in SEQ ID NO. 67 and CDR-H3 as depicted in SEQ ID NO. 68;

(e) CDR-H1 as depicted in SEQ ID NO. 84, CDR-H2 as depicted in SEQ ID NO. 85 and CDR-H3 as depicted in SEQ ID NO. 86;

(f) CDR-H1 as depicted in SEQ ID NO. 102, CDR-H2 as depicted in SEQ ID NO. 103 and CDR-H3 as depicted in SEQ ID NO. 104;

(g) CDR-H1 as depicted in SEQ ID NO. 120, CDR-H2 as depicted in SEQ ID NO. 121 and CDR-H3 as depicted in SEQ ID NO. 122;

(h) CDR-H1 as depicted in SEQ ID NO. 138, CDR-H2 as depicted in SEQ ID NO. 139 and CDR-H3 as depicted in SEQ ID NO. 140;

(i) CDR-H1 as depicted in SEQ ID NO. 156, CDR-H2 as depicted in SEQ ID NO. 157 and CDR-H3 as depicted in SEQ ID NO. 158; and

(j) CDR-H1 as depicted in SEQ ID NO. 174, CDR-H2 as depicted in SEQ ID NO. 175 and CDR-H3 as depicted in SEQ ID NO. 176.

5. The bispecific single chain antibody molecule according to any one of items 1 to 3, wherein the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 ϵ chain comprises a VL region selected from the group consisting of a VL region as depicted in SEQ ID NO. 35, 39, 125, 129, 161 or 165.

6. The bispecific single chain antibody molecule according to any one of items 1 or 2 and 4, wherein the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 ϵ chain comprises a VH region selected from the group consisting of a VH region as depicted in SEQ ID NO. 15, 19, 33, 37, 51, 55, 69, 73, 87, 91, 105, 109, 123, 127, 141, 145, 159, 163, 177 or 181.

7. The bispecific single chain antibody molecule according to any one of items 1 to 6, wherein the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 ϵ chain comprises a VL region and a VH region selected from the group consisting of:

- (a) a VL region as depicted in SEQ ID NO. 17 or 21 and a VH region as depicted in SEQ ID NO. 15 or 19;
- (b) a VL region as depicted in SEQ ID NO. 35 or 39 and a VH region as depicted in SEQ ID NO. 33 or 37;
- (c) a VL region as depicted in SEQ ID NO. 53 or 57 and a VH region as depicted in SEQ ID NO. 51 or 55;
- (d) a VL region as depicted in SEQ ID NO. 71 or 75 and a VH region as depicted in SEQ ID NO. 69 or 73;
- (e) a VL region as depicted in SEQ ID NO. 89 or 93 and a VH region as depicted in SEQ ID NO. 87 or 91;
- (f) a VL region as depicted in SEQ ID NO. 107 or 111 and a VH region as depicted in SEQ ID NO. 105 or 109;
- (g) a VL region as depicted in SEQ ID NO. 125 or 129 and a VH region as depicted in SEQ ID NO. 123 or 127;
- (h) a VL region as depicted in SEQ ID NO. 143 or 147 and a VH region as depicted in SEQ ID NO. 141 or 145;
- (i) a VL region as depicted in SEQ ID NO. 161 or 165 and a VH region as depicted in SEQ ID NO. 159 or 163; and
- (j) a VL region as depicted in SEQ ID NO. 179 or 183 and a VH region as depicted in SEQ ID NO. 177 or 181.

8. The bispecific single chain antibody molecule according to item 7, wherein the first binding domain capable of binding to an epitope of human and non-chimpanzee primate CD3 ϵ chain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 23, 25, 41, 43, 59, 61, 77, 79, 95, 97, 113, 115, 131, 133, 149, 151, 167, 169, 185 or 187.

9. The bispecific single chain antibody molecule according to any one of items 1 to 8, wherein the second binding domain is capable of binding to human PSMA and/or a non-Chimpanzee primate PSMA.

10. The bispecific single chain antibody molecule according to item 9, wherein the bispecific single chain antibody molecule comprises a group of the following sequences as CDR H1, CDR H2, CDR H3, CDR L1, CDR L2 and CDR L3 in the second binding domain selected from:

- a) CDR H1-3 of SEQ ID NO: 394 - 396 and CDR L1-3 of SEQ ID NO: 389 - 391;
- b) CDR H1-3 of SEQ ID NO: 408 - 410 and CDR L1-3 of SEQ ID NO: 403 - 405;
- c) CDR H1-3 of SEQ ID NO: 422 - 424 and CDR L1-3 of SEQ ID NO: 417 - 419;
- d) CDR H1-3 of SEQ ID NO: 436 - 438 and CDR L1-3 of SEQ ID NO: 431 - 433;
- e) CDR H1-3 of SEQ ID NO: 445 - 447 and CDR L1-3 of SEQ ID NO: 450 - 452;
- f) CDR H1-3 of SEQ ID NO: 464 - 466 and CDR L1-3 of SEQ ID NO: 459 - 461;
- g) CDR H1-3 of SEQ ID NO: 478 - 480 and CDR L1-3 of SEQ ID NO: 473 - 475;
- h) CDR H1-3 of SEQ ID NO: 492 - 494 and CDR L1-3 of SEQ ID NO: 487 - 489;
- i) CDR H1-3 of SEQ ID NO: 506 - 508 and CDR L1-3 of SEQ ID NO: 501 - 503;
- j) CDR H1-3 of SEQ ID NO: 520 - 522 and CDR L1-3 of SEQ ID NO: 515 - 517;
- k) CDR H1-3 of SEQ ID NO: 534 - 536 and CDR L1-3 of SEQ ID NO: 529 - 531;
- l) CDR H1-3 of SEQ ID NO: 548 - 550 and CDR L1-3 of SEQ ID NO: 543 - 545;
- m) CDR H1-3 of SEQ ID NO: 562 - 564 and CDR L1-3 of SEQ ID NO: 557 - 559;
- n) CDR H1-3 of SEQ ID NO: 576 - 578 and CDR L1-3 of SEQ ID NO: 571 - 573;
- o) CDR H1-3 of SEQ ID NO: 590 - 592 and CDR L1-3 of SEQ ID NO: 585 - 587;
- p) CDR H1-3 of SEQ ID NO: 604 - 606 and CDR L1-3 of SEQ ID NO: 599 - 601;
- q) CDR H1-3 of SEQ ID NO: 618 - 620 and CDR L1-3 of SEQ ID NO: 613 - 615;
- r) CDR H1-3 of SEQ ID NO: 632 - 634 and CDR L1-3 of SEQ ID NO: 627 - 629;
- s) CDR H1-3 of SEQ ID NO: 646 - 648 and CDR L1-3 of SEQ ID NO: 641 - 643;
- t) CDR H1-3 of SEQ ID NO: 660 - 662 and CDR L1-3 of SEQ ID NO: 655 - 657;
- u) CDR H1-3 of SEQ ID NO: 674 - 676 and CDR L1-3 of SEQ ID NO: 669 - 671;
- v) CDR H1-3 of SEQ ID NO: 688 - 690 and CDR L1-3 of SEQ ID NO: 683 - 685;
- w) CDR H1-3 of SEQ ID NO: 702 - 704 and CDR L1-3 of SEQ ID NO: 697 - 699;
- x) CDR H1-3 of SEQ ID NO: 716 - 718 and CDR L1-3 of SEQ ID NO: 711 - 713;
- y) CDR H1-3 of SEQ ID NO: 729 - 731 and CDR L1-3 of SEQ ID NO: 724 - 726;
- z) CDR H1-3 of SEQ ID NO: 788 - 790 and CDR L1-3 of SEQ ID NO: 793 - 795;
- aa) CDR H1-3 of SEQ ID NO: 806 - 808 and CDR L1-3 of SEQ ID NO: 811 - 813;
- ab) CDR H1-3 of SEQ ID NO: 852 - 854 and CDR L1-3 of SEQ ID NO: 857 - 859;
- ac) CDR H1-3 of SEQ ID NO: 838 - 840 and CDR L1-3 of SEQ ID NO: 843 - 845;
- ad) CDR H1-3 of SEQ ID NO: 824 - 826 and CDR L1-3 of SEQ ID NO: 829 - 831;
- ae) CDR H1-3 of SEQ ID NO: 774 - 776 and CDR L1-3 of SEQ ID NO: 779 - 781;
- af) CDR H1-3 of SEQ ID NO: 688 - 690 and CDR L1-3 of SEQ ID NO: 683 - 685;
- ag) CDR H1-3 of SEQ ID NO: 870 - 872 and CDR L1-3 of SEQ ID NO: 875 - 877;
- ah) CDR H1-3 of SEQ ID NO: 888 - 890 and CDR L1-3 of SEQ ID NO: 893 - 895;
- ai) CDR H1-3 of SEQ ID NO: 924 - 926 and CDR L1-3 of SEQ ID NO: 929 - 931;

- aj) CDR H1-3 of SEQ ID NO: 1019 - 1021 and CDR L1-3 of SEQ ID NO: 1025 - 1027;
- ak) CDR H1-3 of SEQ ID NO: 1006 - 1008 and CDR L1-3 of SEQ ID NO: 1011 - 1013;
- al) CDR H1-3 of SEQ ID NO: 906 - 908 and CDR L1-3 of SEQ ID NO: 911 - 913;
- am) CDR H1-3 of SEQ ID NO: 992 - 994 and CDR L1-3 of SEQ ID NO: 997 - 999;
- an) CDR H1-3 of SEQ ID NO: 942 - 944 and CDR L1-3 of SEQ ID NO: 947 - 949;
- ao) CDR H1-3 of SEQ ID NO: 960 - 962 and CDR L1-3 of SEQ ID NO: 965 - 967; and
- ap) CDR H1-3 of SEQ ID NO: 978 - 980 and CDR L1-3 of SEQ ID NO: 983 - 985.

11. The bispecific single chain antibody molecule of item 10, wherein the binding domains are arranged in the order VH PSMA-VL PSMA-VH CD3-VL CD3 or VL PSMA-VH PSMA-VH CD3-VL CD3.

12. The bispecific single chain antibody molecule according to item 11, wherein the bispecific single chain antibody molecule comprises a sequence selected from:

- (a) an amino acid sequence as depicted in any of SEQ ID NOs: 399, 413, 427, 441, 455, 469, 483, 497, 511, 525, 539, 553, 567, 581, 595, 609, 623, 637, 651, 665, 679, 693, 707, 721, 734, 799, 817, 863, 849, 835, 785, 899, 935, 1017, 1031, 917, 1003, 953, 971 or 989;
- (b) an amino acid sequence encoded by a nucleic acid sequence as depicted in any of SEQ ID NOs: 400, 414, 428, 442, 456, 470, 484, 498, 512, 526, 540, 554, 568, 582, 596, 610, 624, 638, 652, 666, 680, 694, 708, 736, 735, 800, 818, 864, 850, 836, 786, 882, 900, 936, 1018, 1032, 918, 1004, 954, 972, 990, 804, 822, 868, 886, 904, 940, 922, 958 or 976; and
- (c) an amino acid sequence at least 90 % identical, more preferred at least 95 % identical, most preferred at least 96 % identical to the amino acid sequence of (a) or (b).

13. A nucleic acid sequence encoding a bispecific single chain antibody molecule as defined in any of items 1 to 12.

14. A vector, which comprises a nucleic acid sequence as defined in item 13.

15. The vector of item 14, wherein said vector further comprises a regulatory sequence, which is operably linked to said nucleic acid sequence defined in item 13.

16. The vector of item 15, wherein said vector is an expression vector.

17. A host transformed or transfected with a vector defined in any of items 14 to 16.

18. A process for the production of a bispecific single chain antibody molecule according to any of items 1 to 12, said process comprising culturing a host defined in item 17 under conditions allowing the expression of the bispecific single chain antibody molecule as defined in any of items 1 to 12 and recovering the produced polypeptide from the culture.

19. A pharmaceutical composition comprising a bispecific single chain antibody molecule according to any one of items 1 to 12, or produced according to the process of item 18.

20. The pharmaceutical composition of item 19 for use in the prevention, treatment or amelioration of cancer.

21. A bispecific single chain antibody molecule according to any one of items 1 to 12, or produced according to the process of item 18, for use in the prevention, treatment or amelioration of cancer.

22. The pharmaceutical composition of item 20 or the bispecific single chain antibody molecule of item 21, wherein said cancer is a solid tumor, preferably a carcinoma or prostate cancer.

23. The pharmaceutical composition of item 19, 20 or 22 or the bispecific single chain antibody molecule of item 21 or 22 which, optionally further comprises suitable formulations of carriers, stabilizers and/or excipients.

24. The pharmaceutical composition of item 19, 20, 22 or 23 or the bispecific single chain antibody molecule of item 21, 22 or 23, wherein said bispecific single chain antibody molecule or pharmaceutical composition is suitable to be administered in combination with an additional drug.

25. The pharmaceutical composition or bispecific single chain antibody molecule of item 24, wherein said drug is a non-proteinaceous compound or a proteinaceous compound.

26. The pharmaceutical composition or the bispecific single chain antibody molecule of item 25, wherein said proteinaceous compound or non-proteinaceous compound is administered simultaneously or non-simultaneously with the bispecific single chain antibody molecule of item 21, 22, or 23, or the pharmaceutical composition according to item 19 or 20.

27. Use of a bispecific single chain antibody molecule as defined in any of items 1 to 12, or produced according to item 18, for the preparation of a pharmaceutical composition for the prevention, treatment or amelioration of a disease.

28. A method for the prevention, treatment or amelioration of a disease in a subject in the need thereof, said method comprising the step of administration of an effective amount of a pharmaceutical composition of item 19 or 20.

29. The method of item 28 or the use of item 27, wherein said disease is cancer.

30. The method or use of item 29, wherein said cancer is a solid tumor, preferably a carcinoma or prostate cancer.

31. The method of any of items 28 to 30 or the use of item 27, 29 or 30, wherein said pharmaceutical composition is administered in combination with an additional drug.

32. The method or use of item 31, wherein said drug is a non-proteinaceous compound or a proteinaceous compound.

33. The method or use of item 32, wherein said proteinaceous compound or non-proteinaceous compound is administered simultaneously or non-simultaneously with a pharmaceutical composition according to item 19 or 20.

34. The method of any one of items 28 to 33 or the use of item 27, or 29 to 33, wherein said subject is a human.

35. A kit comprising a bispecific single chain antibody molecule as defined in any of items 1 to 12, a nucleic acid molecule as defined in item 13, a vector as defined in any of items 14 to 16, or a host as defined in item 17.

Claims

1. A bispecific single chain antibody molecule comprising a first binding domain which specifically binds to an epitope of human and *Callithrix jacchus*, *Saguinus oedipus* or *Saimiri sciureus* CD3 ϵ (epsilon) chain, wherein said epitope is part of an amino acid sequence comprised in the group consisting of SEQ ID NOs. 2, 4, 6, or 8, and comprises at least the amino acid sequence Gln-Asp-Gly-Asn-Glu, and a second binding domain binding to prostate-specific membrane antigen (PSMA) for use in a method for killing PSMA-expressing human prostate cancer cells.

2. The bispecific single chain antibody molecule for the use according to claim 1, wherein the first binding domain comprises a VL region comprising CDR-L1, CDR-L2 and CDR-L3 selected from:

(a) CDR-L1 as depicted in SEQ ID NO. 27, CDR-L2 as depicted in SEQ ID NO. 28 and CDR-L3 as depicted in SEQ ID NO. 29;

(b) CDR-L1 as depicted in SEQ ID NO. 117, CDR-L2 as depicted in SEQ ID NO. 118 and CDR-L3 as depicted in SEQ ID NO. 119; and

(c) CDR-L1 as depicted in SEQ ID NO. 153, CDR-L2 as depicted in SEQ ID NO. 154 and CDR-L3 as depicted in SEQ ID NO. 155.

3. The bispecific single chain antibody molecule for the use according to claim 1 or 2, wherein the first binding domain comprises a VH region comprising CDR-H1, CDR-H2 and CDR-H3 selected from:

(a) CDR-H1 as depicted in SEQ ID NO. 12, CDR-H2 as depicted in SEQ ID NO. 13 and CDR-H3 as depicted in SEQ ID NO. 14;

(b) CDR-H1 as depicted in SEQ ID NO. 30, CDR-H2 as depicted in SEQ ID NO. 31 and CDR-H3 as depicted in SEQ ID NO. 32;

(c) CDR-H1 as depicted in SEQ ID NO. 48, CDR-H2 as depicted in SEQ ID NO. 49 and CDR-H3 as depicted

in SEQ ID NO. 50;

(d) CDR-H1 as depicted in SEQ ID NO. 66, CDR-H2 as depicted in SEQ ID NO. 67 and CDR-H3 as depicted in SEQ ID NO. 68;

(e) CDR-H1 as depicted in SEQ ID NO. 84, CDR-H2 as depicted in SEQ ID NO. 85 and CDR-H3 as depicted in SEQ ID NO. 86;

(f) CDR-H1 as depicted in SEQ ID NO. 102, CDR-H2 as depicted in SEQ ID NO. 103 and CDR-H3 as depicted in SEQ ID NO. 104;

(g) CDR-H1 as depicted in SEQ ID NO. 120, CDR-H2 as depicted in SEQ ID NO. 121 and CDR-H3 as depicted in SEQ ID NO. 122;

(h) CDR-H1 as depicted in SEQ ID NO. 138, CDR-H2 as depicted in SEQ ID NO. 139 and CDR-H3 as depicted in SEQ ID NO. 140;

(i) CDR-H1 as depicted in SEQ ID NO. 156, CDR-H2 as depicted in SEQ ID NO. 157 and CDR-H3 as depicted in SEQ ID NO. 158; and

(j) CDR-H1 as depicted in SEQ ID NO. 174, CDR-H2 as depicted in SEQ ID NO. 175 and CDR-H3 as depicted in SEQ ID NO. 176.

4. The bispecific single chain antibody molecule for the use according to any one of claims 1 to 3, wherein the second binding domain is capable of binding to human PSMA and/or a non-human primate PSMA.

5. The bispecific single chain antibody molecule for the use according to claim 4, wherein the bispecific single chain antibody molecule comprises a group of the following sequences as CDR H1, CDR H2, CDR H3, CDR L1, CDR L2 and CDR L3 in the second binding domain selected from:

a) CDR H1-3 of SEQ ID NO: 394 - 396 and CDR L1-3 of SEQ ID NO: 389 - 391;

b) CDR H1-3 of SEQ ID NO: 408 - 410 and CDR L1-3 of SEQ ID NO: 403 - 405;

c) CDR H1-3 of SEQ ID NO: 422 - 424 and CDR L1-3 of SEQ ID NO: 417 - 419;

d) CDR H1-3 of SEQ ID NO: 436 - 438 and CDR L1-3 of SEQ ID NO: 431 - 433;

e) CDR H1-3 of SEQ ID NO: 445 - 447 and CDR L1-3 of SEQ ID NO: 450 - 452;

f) CDR H1-3 of SEQ ID NO: 464 - 466 and CDR L1-3 of SEQ ID NO: 459 - 461;

g) CDR H1-3 of SEQ ID NO: 478 - 480 and CDR L1-3 of SEQ ID NO: 473 - 475;

h) CDR H1-3 of SEQ ID NO: 492 - 494 and CDR L1-3 of SEQ ID NO: 487 - 489;

i) CDR H1-3 of SEQ ID NO: 506 - 508 and CDR L1-3 of SEQ ID NO: 501 - 503;

j) CDR H1-3 of SEQ ID NO: 520 - 522 and CDR L1-3 of SEQ ID NO: 515 - 517;

k) CDR H1-3 of SEQ ID NO: 534 - 536 and CDR L1-3 of SEQ ID NO: 529 - 531;

l) CDR H1-3 of SEQ ID NO: 548 - 550 and CDR L1-3 of SEQ ID NO: 543 - 545;

m) CDR H1-3 of SEQ ID NO: 562 - 564 and CDR L1-3 of SEQ ID NO: 557 - 559;

n) CDR H1-3 of SEQ ID NO: 576 - 578 and CDR L1-3 of SEQ ID NO: 571 - 573;

o) CDR H1-3 of SEQ ID NO: 590 - 592 and CDR L1-3 of SEQ ID NO: 585 - 587;

p) CDR H1-3 of SEQ ID NO: 604 - 606 and CDR L1-3 of SEQ ID NO: 599 - 601;

q) CDR H1-3 of SEQ ID NO: 618 - 620 and CDR L1-3 of SEQ ID NO: 613 - 615;

r) CDR H1-3 of SEQ ID NO: 632 - 634 and CDR L1-3 of SEQ ID NO: 627 - 629;

s) CDR H1-3 of SEQ ID NO: 646 - 648 and CDR L1-3 of SEQ ID NO: 641 - 643;

t) CDR H1-3 of SEQ ID NO: 660 - 662 and CDR L1-3 of SEQ ID NO: 655 - 657;

u) CDR H1-3 of SEQ ID NO: 674 - 676 and CDR L1-3 of SEQ ID NO: 669 - 671;

v) CDR H1-3 of SEQ ID NO: 688 - 690 and CDR L1-3 of SEQ ID NO: 683 - 685;

w) CDR H1-3 of SEQ ID NO: 702 - 704 and CDR L1-3 of SEQ ID NO: 697 - 699;

x) CDR H1-3 of SEQ ID NO: 716 - 718 and CDR L1-3 of SEQ ID NO: 711 - 713;

y) CDR H1-3 of SEQ ID NO: 729 - 731 and CDR L1-3 of SEQ ID NO: 724 - 726;

z) CDR H1-3 of SEQ ID NO: 788 - 790 and CDR L1-3 of SEQ ID NO: 793 - 795;

aa) CDR H1-3 of SEQ ID NO: 806 - 808 and CDR L1-3 of SEQ ID NO: 811 - 813;

ab) CDR H1-3 of SEQ ID NO: 852 - 854 and CDR L1-3 of SEQ ID NO: 857 - 859;

ac) CDR H1-3 of SEQ ID NO: 838 - 840 and CDR L1-3 of SEQ ID NO: 843 - 845;

ad) CDR H1-3 of SEQ ID NO: 824 - 826 and CDR L1-3 of SEQ ID NO: 829 - 831;

ae) CDR H1-3 of SEQ ID NO: 774 - 776 and CDR L1-3 of SEQ ID NO: 779 - 781;

af) CDR H1-3 of SEQ ID NO: 688 - 690 and CDR L1-3 of SEQ ID NO: 683 - 685;

ag) CDR H1-3 of SEQ ID NO: 870 - 872 and CDR L1-3 of SEQ ID NO: 875 - 877;

ah) CDR H1-3 of SEQ ID NO: 888 - 890 and CDR L1-3 of SEQ ID NO: 893 - 895;

ai) CDR H1-3 of SEQ ID NO: 924 - 926 and CDR L1-3 of SEQ ID NO: 929 - 931;

aj) CDR H1-3 of SEQ ID NO: 1019 - 1021 and CDR L1-3 of SEQ ID NO: 1025 - 1027;
 ak) CDR H1-3 of SEQ ID NO: 1006 - 1008 and CDR L1-3 of SEQ ID NO: 1011 - 1013;
 al) CDR H1-3 of SEQ ID NO: 906 - 908 and CDR L1-3 of SEQ ID NO: 911 - 913;
 am) CDR H1-3 of SEQ ID NO: 992 - 994 and CDR L1-3 of SEQ ID NO: 997 - 999;
 an) CDR H1-3 of SEQ ID NO: 942 - 944 and CDR L1-3 of SEQ ID NO: 947 - 949;
 ao) CDR H1-3 of SEQ ID NO: 960 - 962 and CDR L1-3 of SEQ ID NO: 965 - 967; and
 ap) CDR H1-3 of SEQ ID NO: 978 - 980 and CDR L1-3 of SEQ ID NO: 983 - 985.

6. The bispecific single chain antibody molecule for the use according to claim 5, wherein the binding domains are arranged in the order VH PSMA-VL PSMA-VH CD3-VL CD3 or VL PSMA-VH PSMA-VH CD3-VL CD3.

7. The bispecific single chain antibody molecule for the use according to claim 6, wherein the bispecific single chain antibody molecule comprises a sequence selected from:

(a) an amino acid sequence as depicted in any of SEQ ID NOs: 399, 413, 427, 441, 455, 469, 483, 497, 511, 525, 539, 553, 567, 581, 595, 609, 623, 637, 651, 665, 679, 693, 707, 721, 734, 799, 817, 863, 849, 835, 785, 899, 935, 1017, 1031, 917, 1003, 953, 971 or 989;

(b) an amino acid sequence encoded by a nucleic acid sequence as depicted in any of SEQ ID NOs: 400, 414, 428, 442, 456, 470, 484, 498, 512, 526, 540, 554, 568, 582, 596, 610, 624, 638, 652, 666, 680, 694, 708, 736, 735, 800, 818, 864, 850, 836, 786, 882, 900, 936, 1018, 1032, 918, 1004, 954, 972, 990, 804, 822, 868, 886, 904, 940, 922, 958 or 976; and

(c) an amino acid sequence at least 90 % identical, more preferred at least 95 % identical, most preferred at least 96 % identical to the amino acid sequence of (a) or (b).

8. The bispecific single chain antibody molecule for the use according to any one of claims 1 to 7, wherein said first binding domain or second binding domain of said bispecific single chain antibody molecule is humanized.

9. The bispecific single chain antibody molecule for the use according to any one of claims 1 to 8, wherein said bispecific single chain antibody molecule is administered in combination with an additional drug,

10. The bispecific single chain antibody molecule for the use according to claim 9, wherein said drug is a non-proteinaceous compound or a proteinaceous compound.

11. The bispecific single chain antibody molecule for the use according to claim 10, wherein said proteinaceous compound is capable of providing an activation signal for immune effector cells.

12. The bispecific single chain antibody molecule for the use according to any one of claims 9 to 11, wherein said proteinaceous or non-proteinaceous compound is administered simultaneously or non-simultaneously with said bispecific single chain antibody molecule.

13. A nucleic acid sequence encoding a bispecific single chain antibody molecule as defined in any of claims 1 to 8 for use in a method for killing PSMA-expressing human prostate cancer cells.

14. A vector, which comprises a nucleic acid sequence as defined in claim 13 for use in a method for killing PSMA-expressing human prostate cancer cells.

15. A host cell transformed or transfected with a vector defined in claim 14 for use in a method for killing PSMA-expressing human prostate cancer cells.

Figure 1

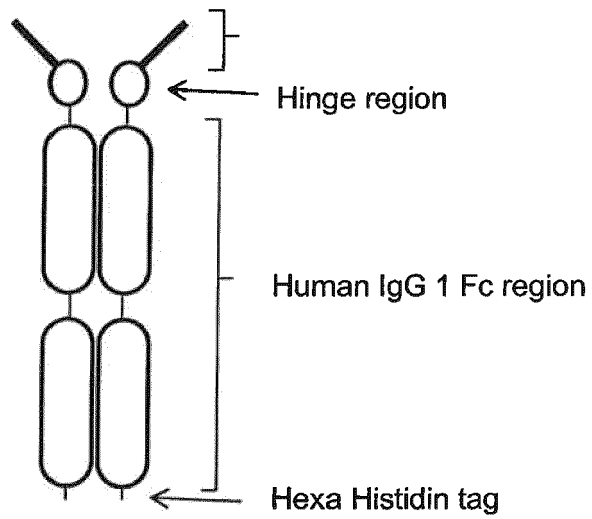


Figure 2

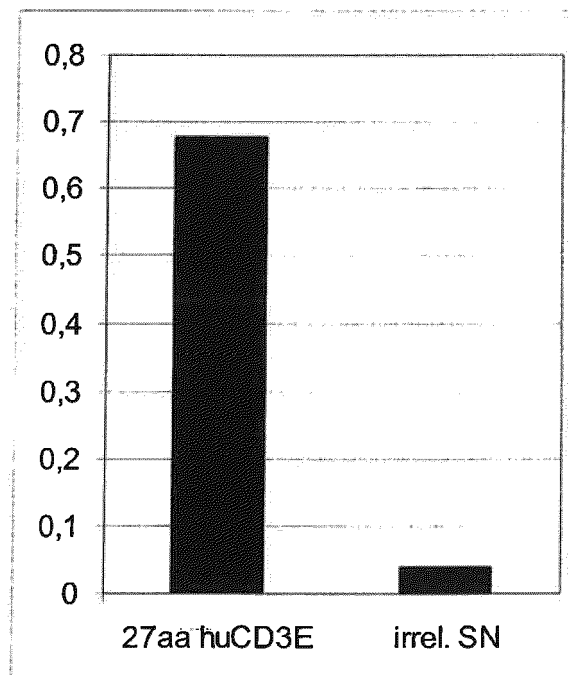


Figure 3

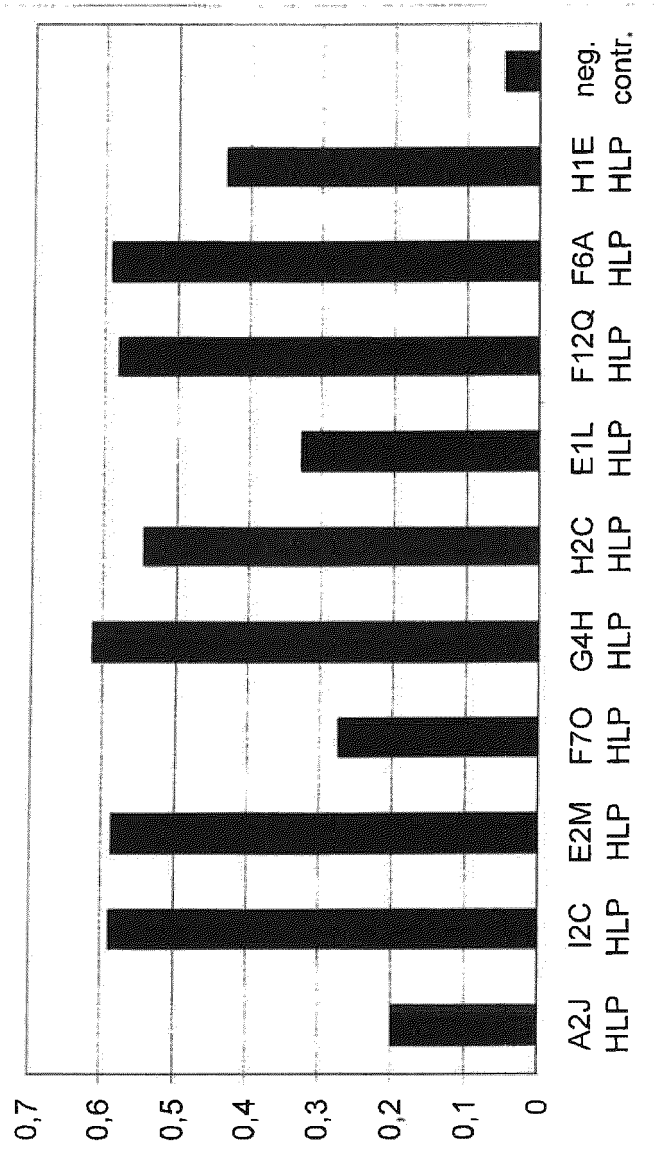


Figure 4

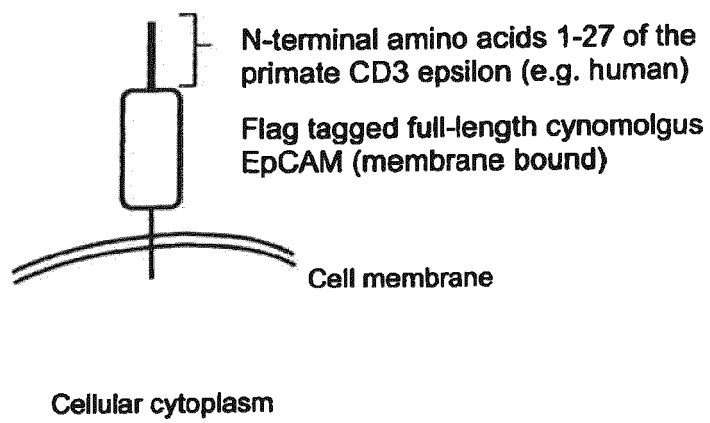


Figure 5

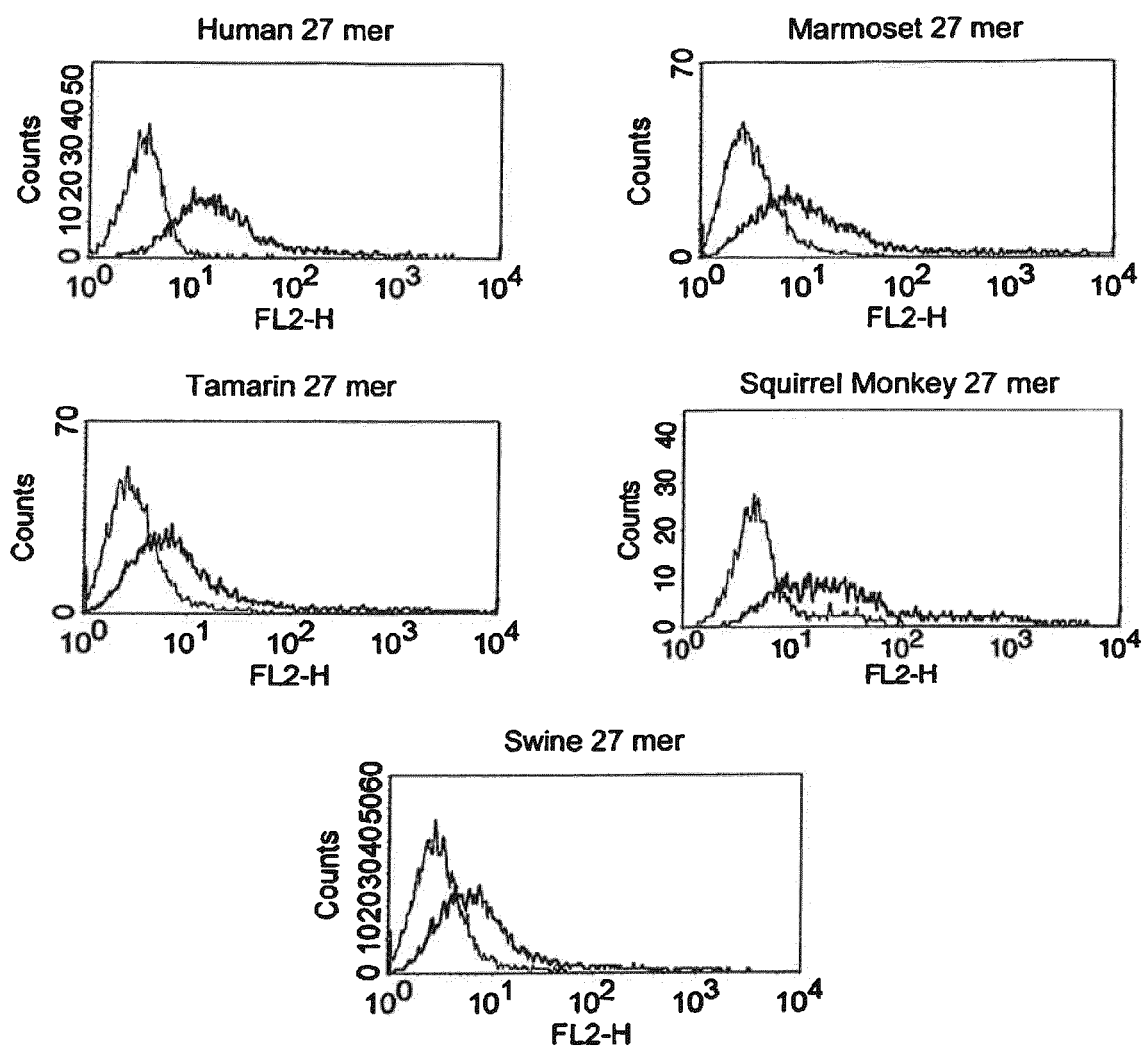


Figure 6A

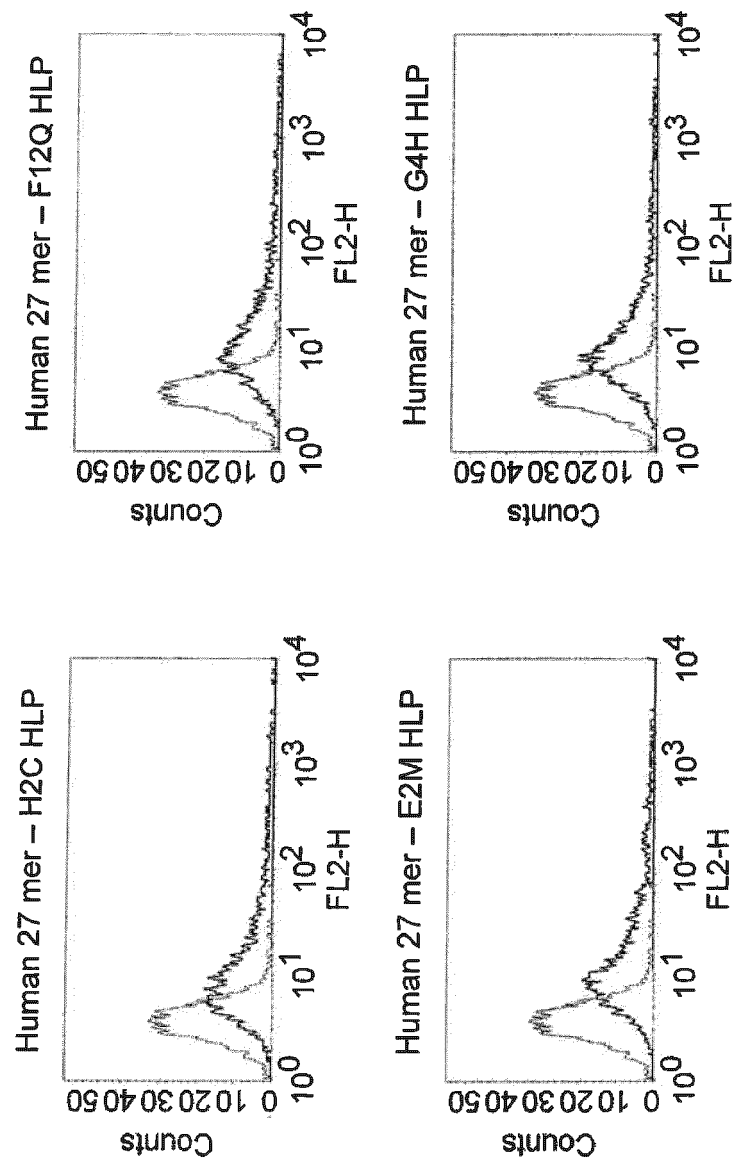


Figure 6B

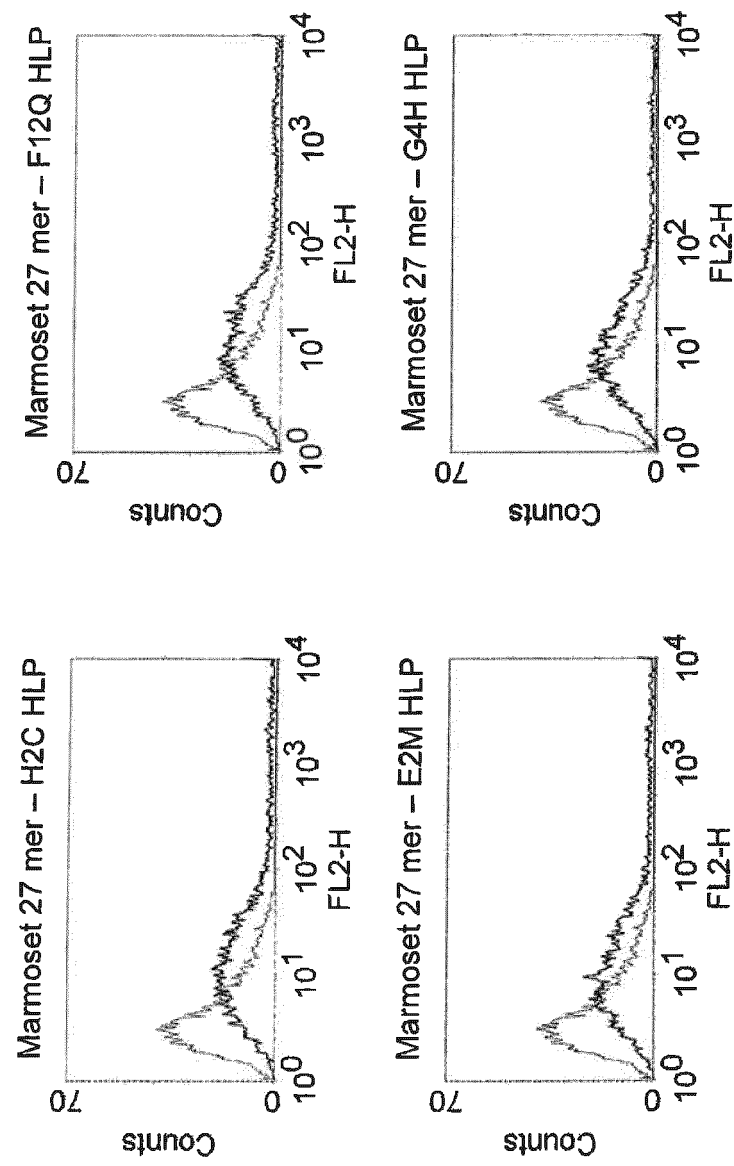


Figure 6C

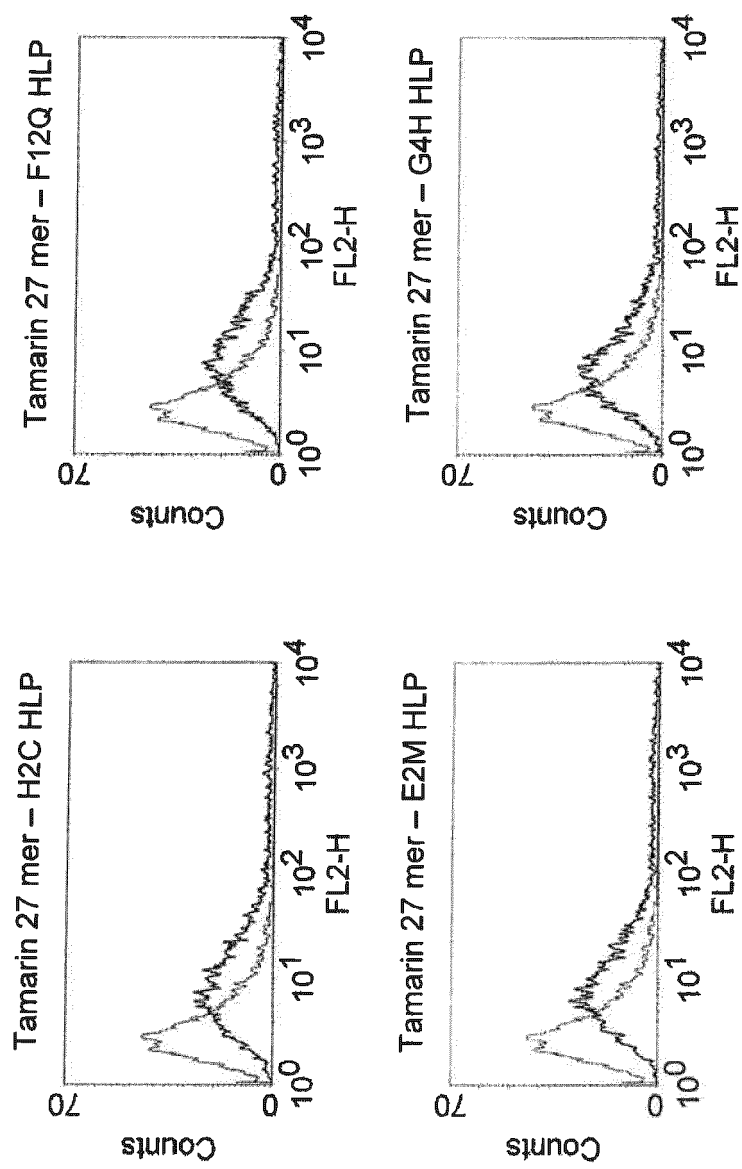


Figure 6D

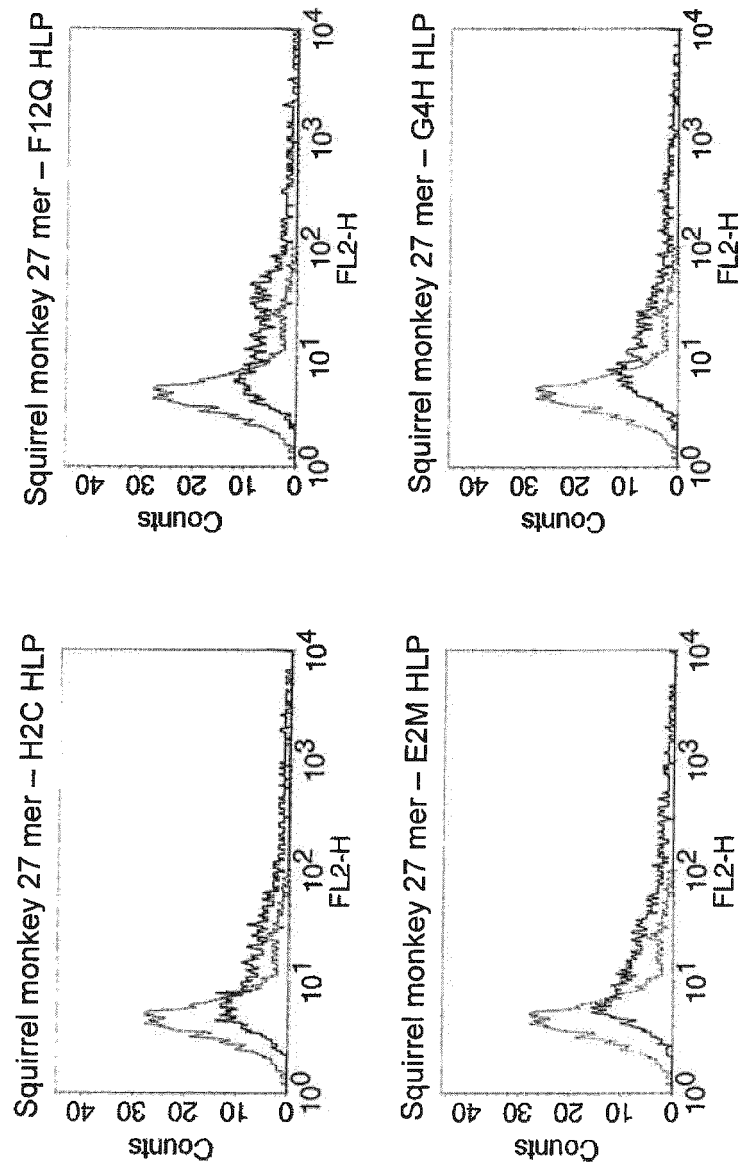


Figure 6E

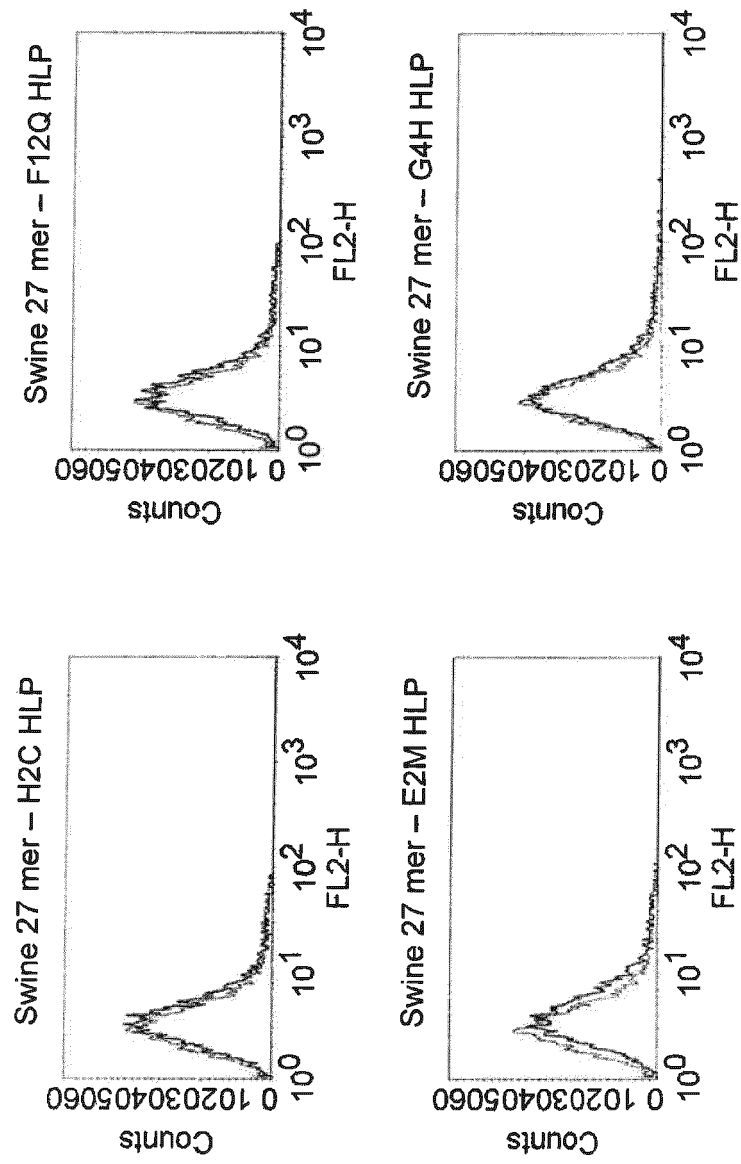


Figure 7

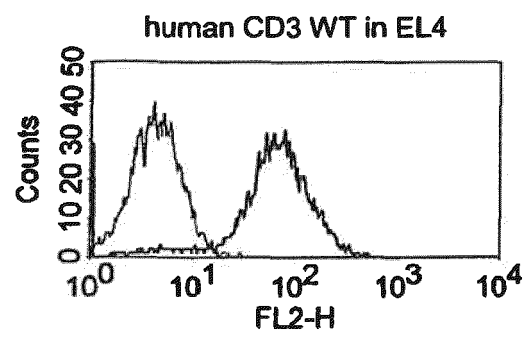


Figure 8A

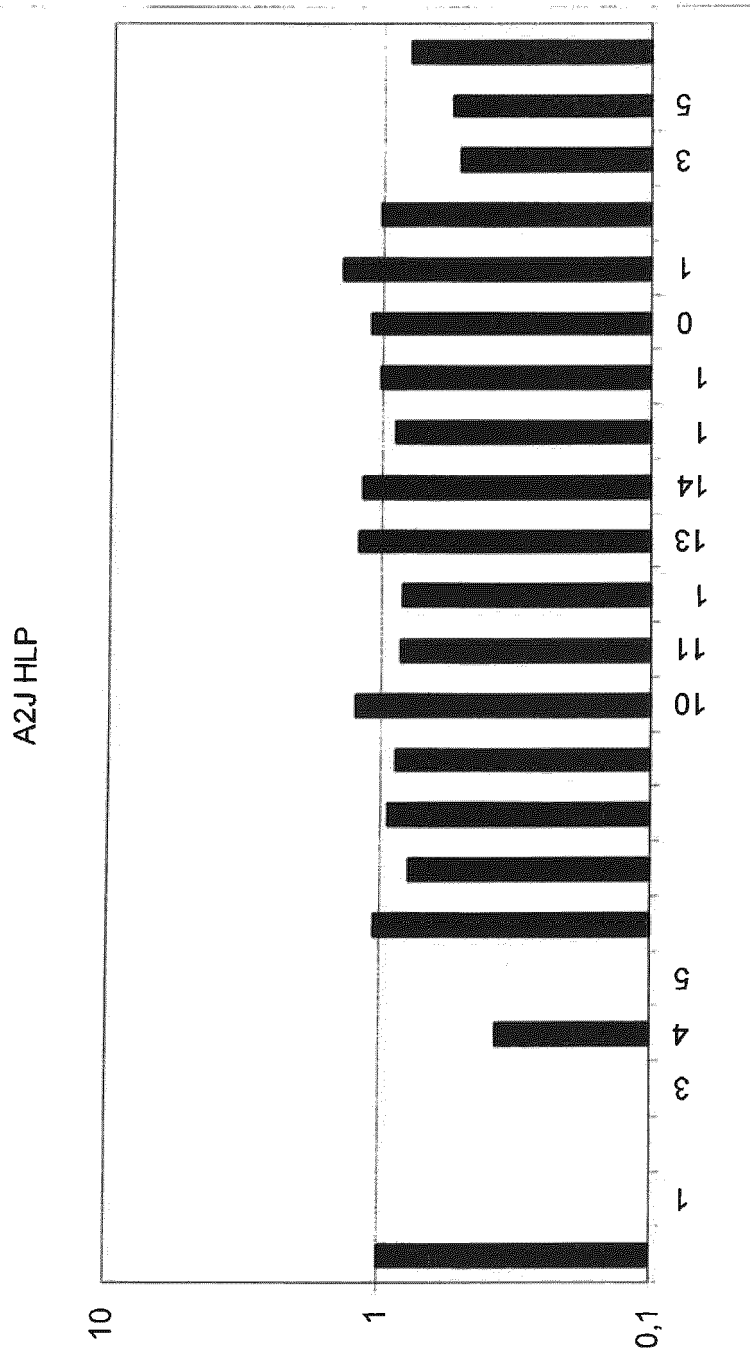


Figure 8B

E2M HLP

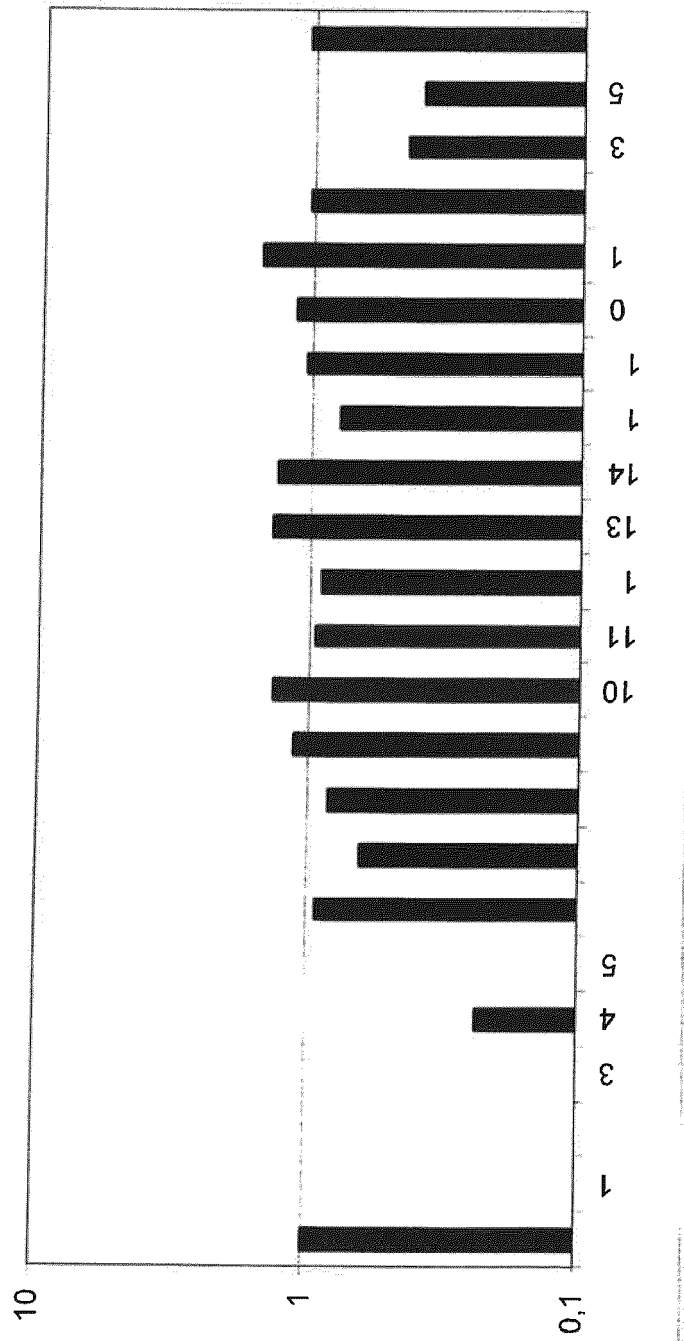


Figure 8C

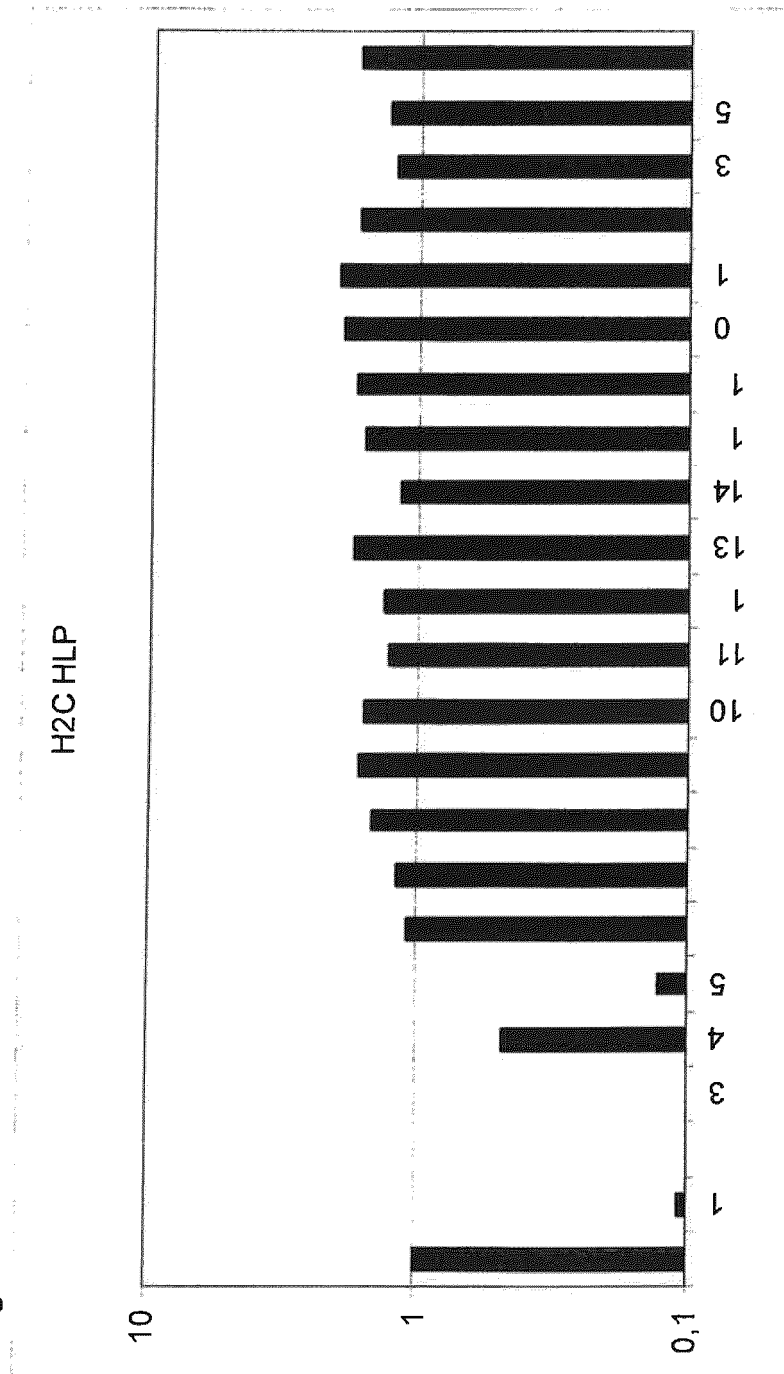


Figure 8D

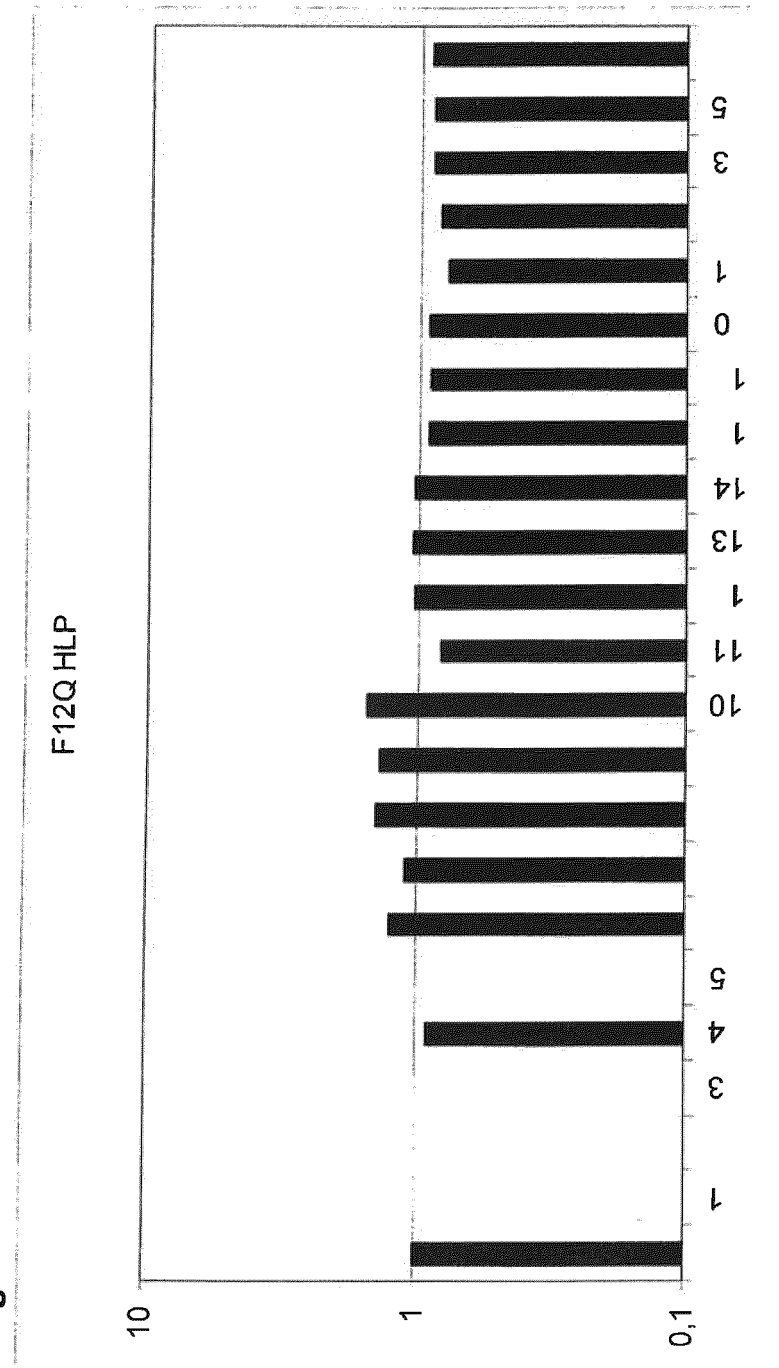


Figure 9

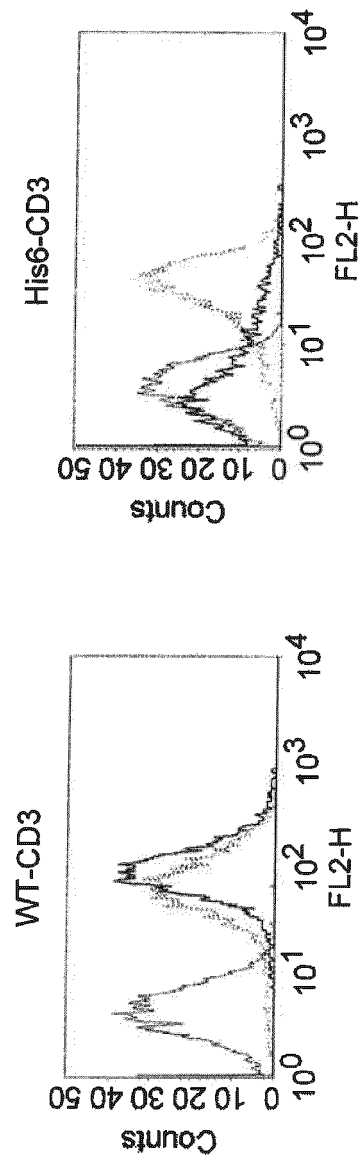


Figure 10

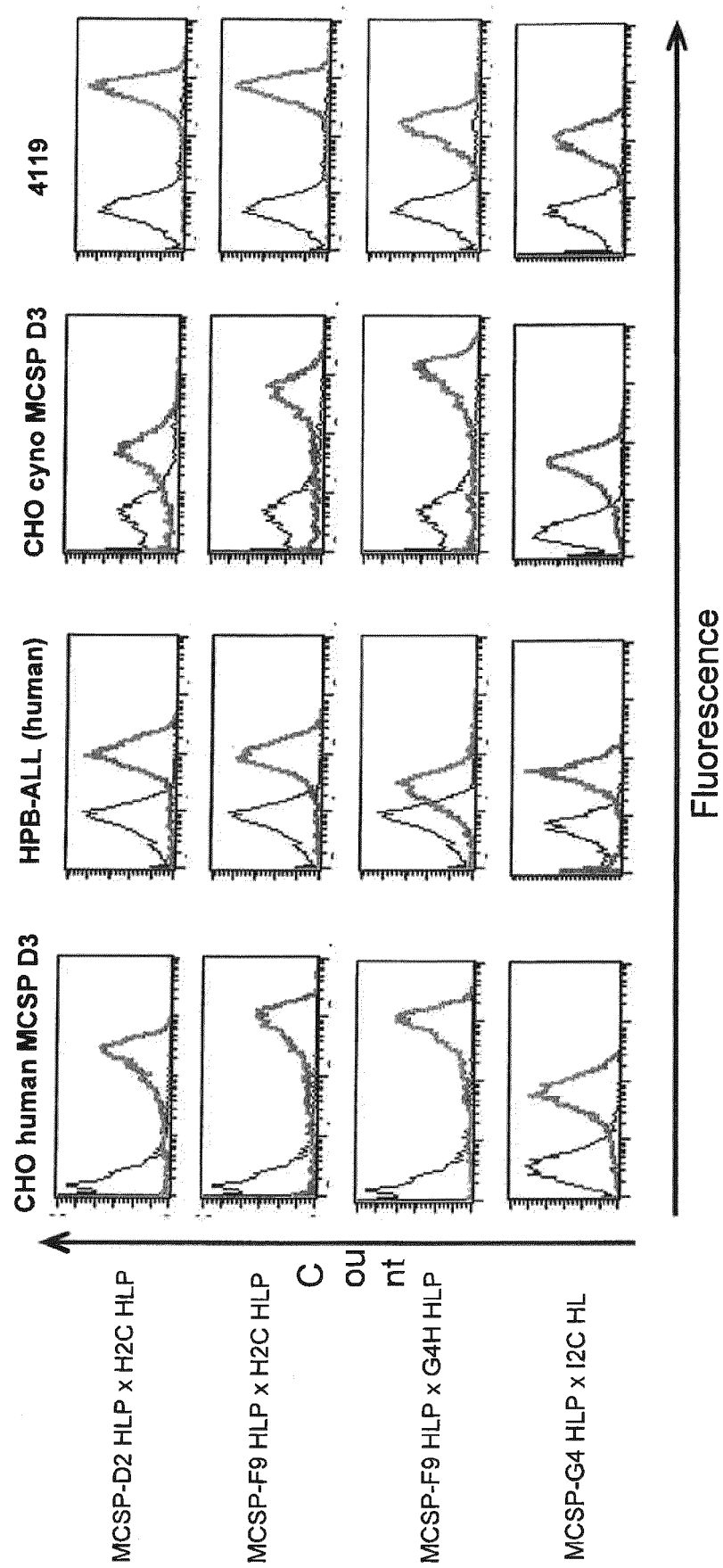


Figure 11

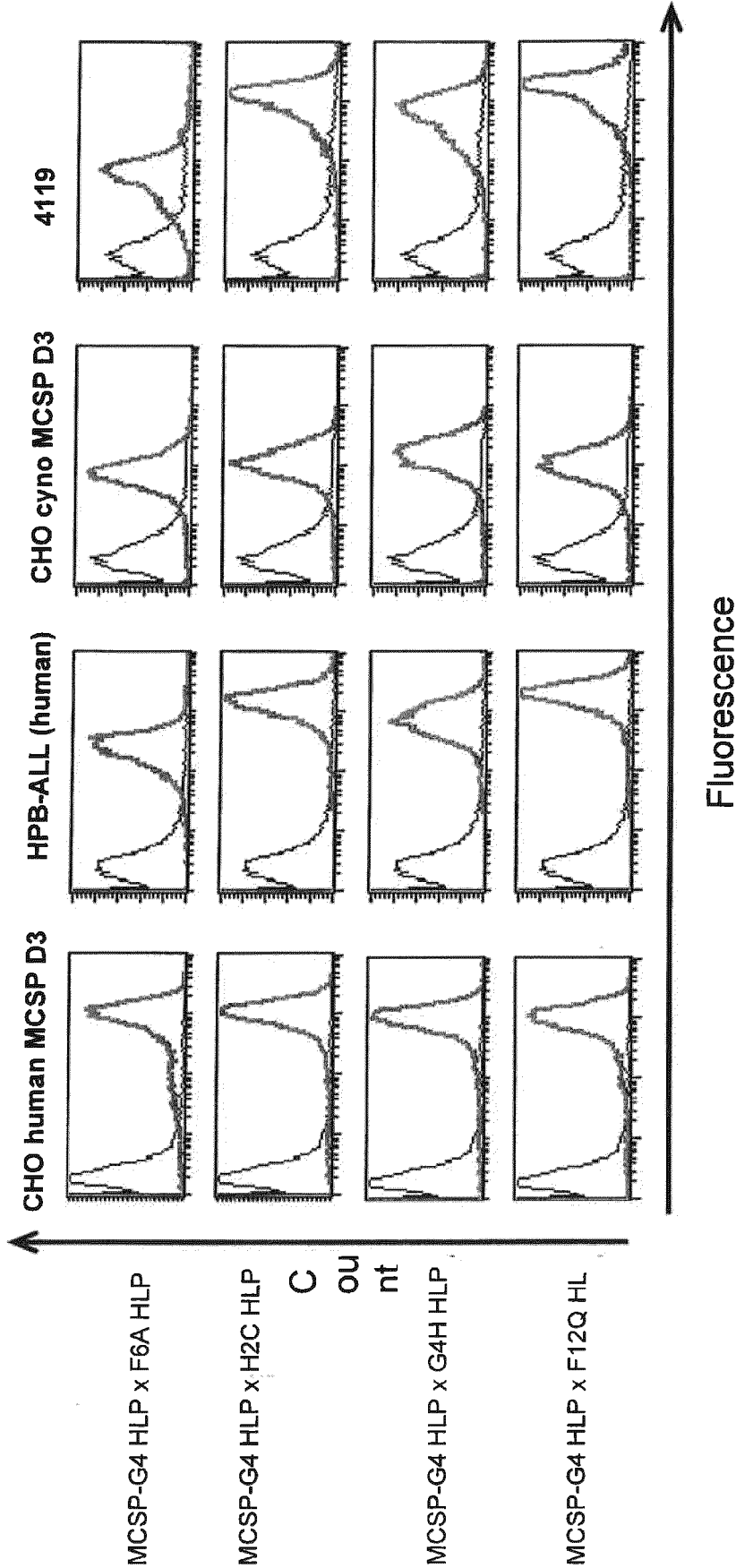


Figure 12

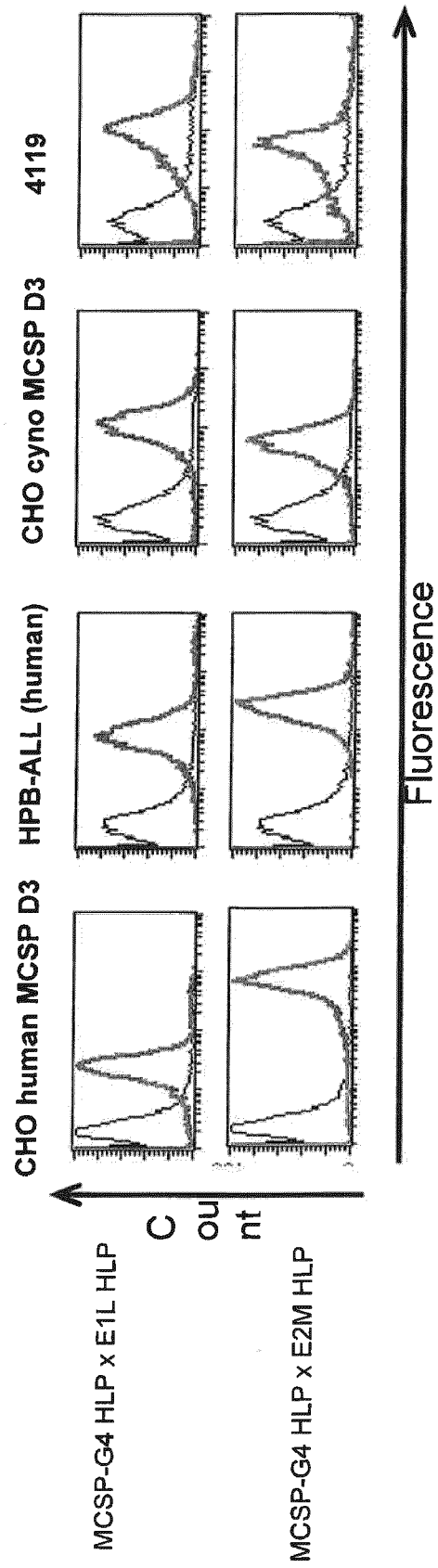
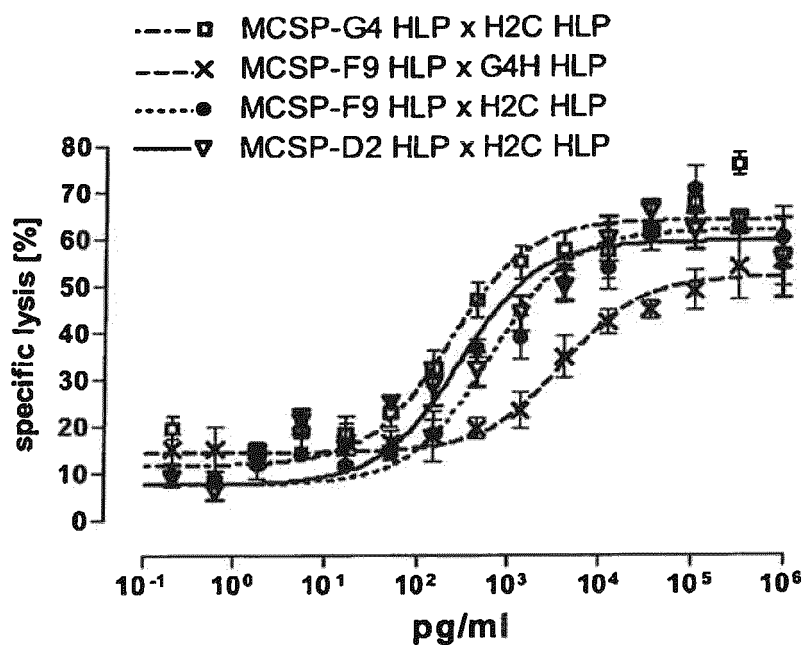


Figure 13

A)

Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human MCSP D3



B)

Effector cells: macaque T cell line 4119 LnPx

Target cells: CHO transfected with cynomolgus MCSP D3

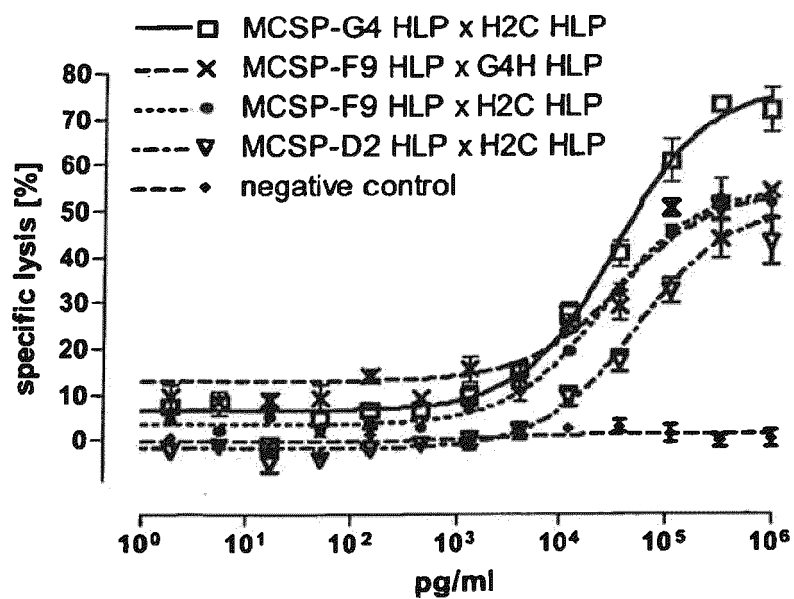
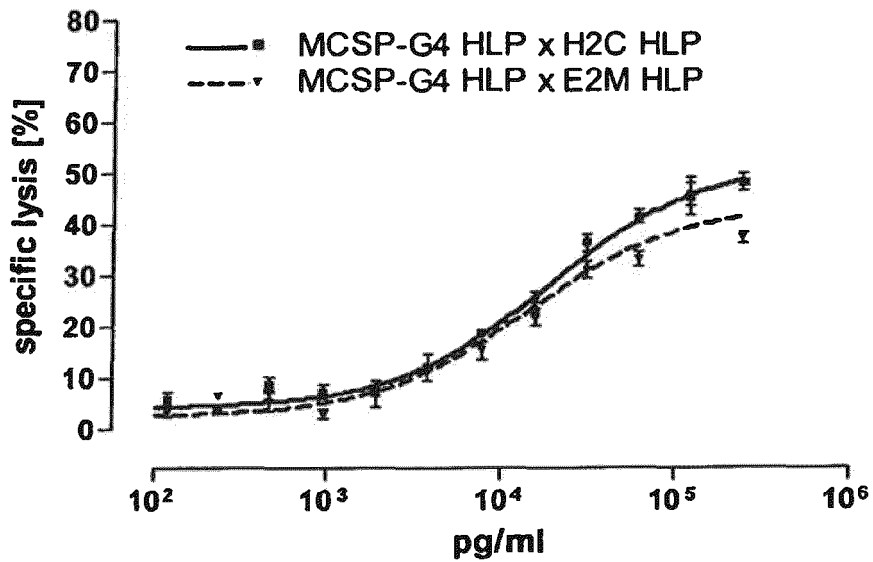


Figure 14

A)

Effector cells: macaque T cell line 4119 LnPx

Target cells: CHO transfected with cynomolgus MCSP D3



B)

Effector cells: macaque T cell line 4119 LnPx

Target cells: CHO transfected with cynomolgus MCSP D3

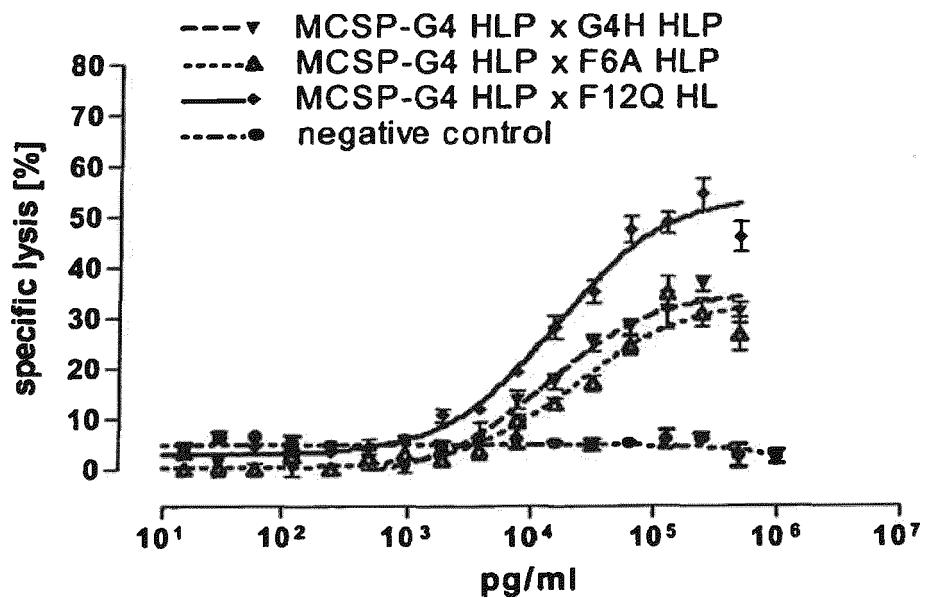
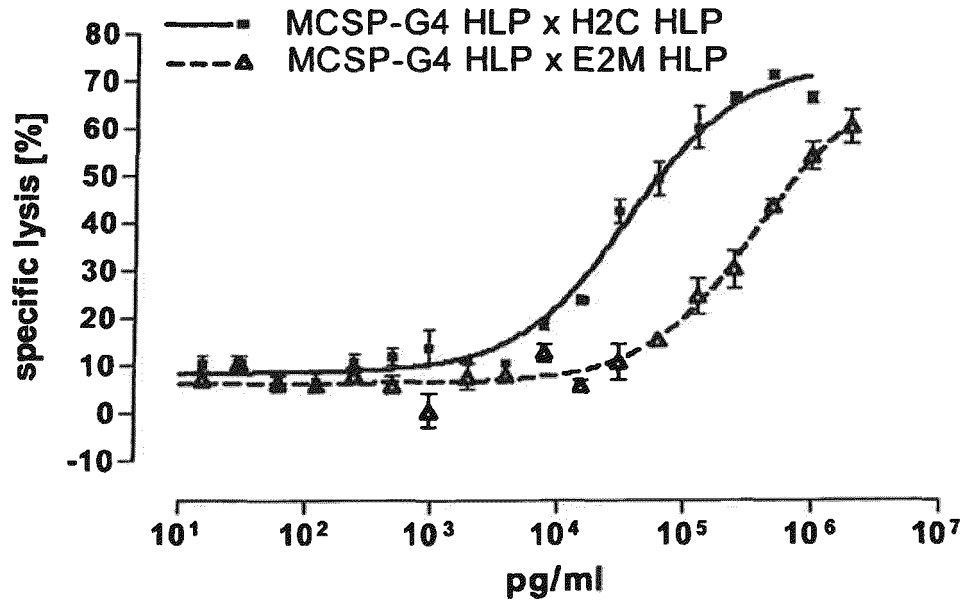


Figure 15

A)

Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human MCSP D3



B)

Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human MCSP D3

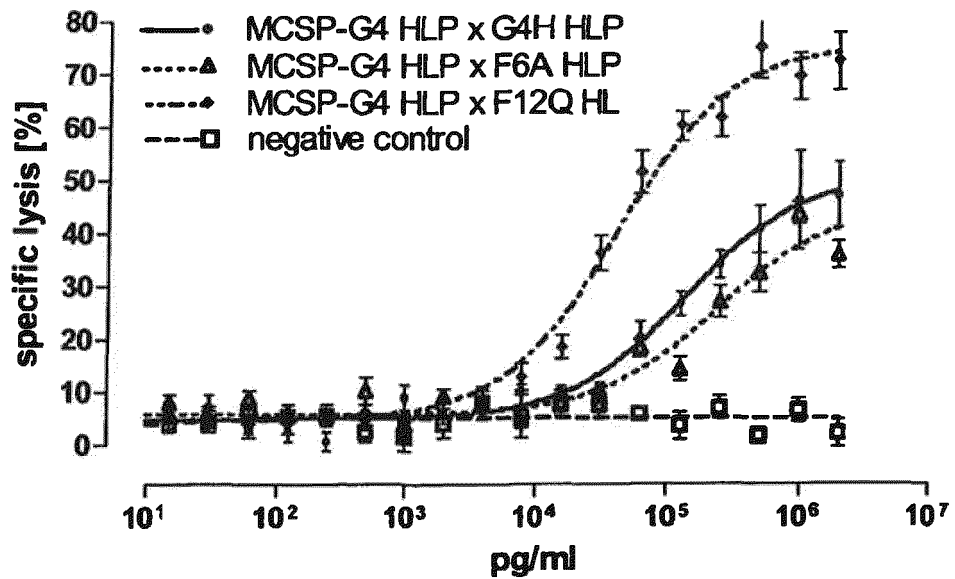
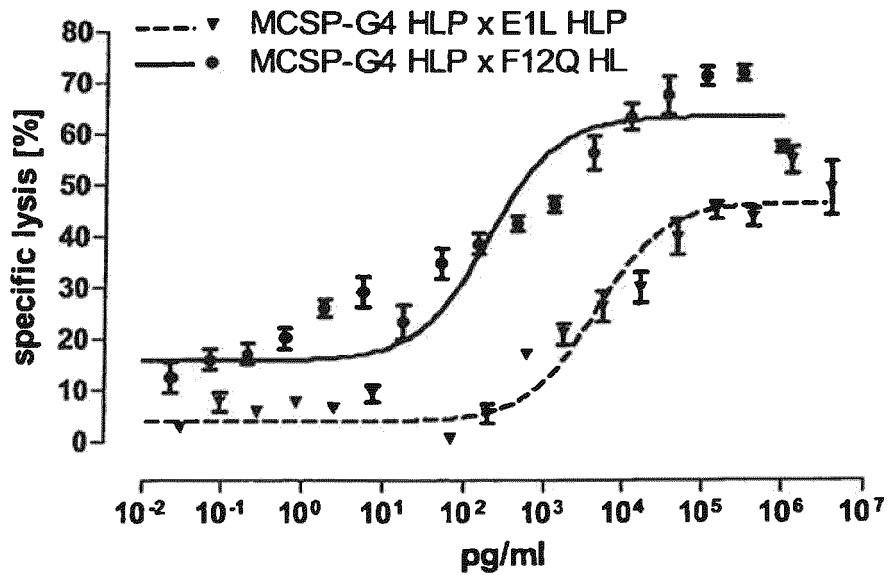


Figure 16

A)

Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human MCSP D3



B)

Effector cells: macaque T cell line 4119 LnPx

Target cells: CHO transfected with cynomolgus MCSP D

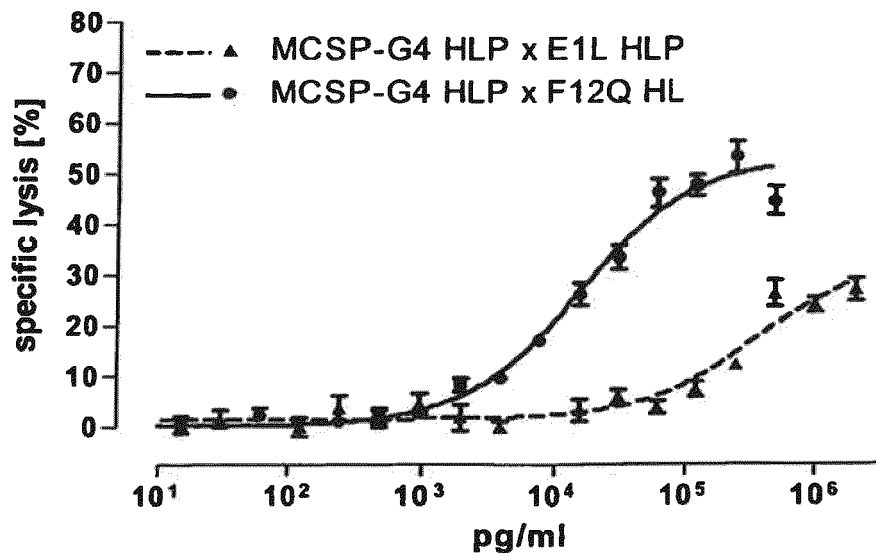
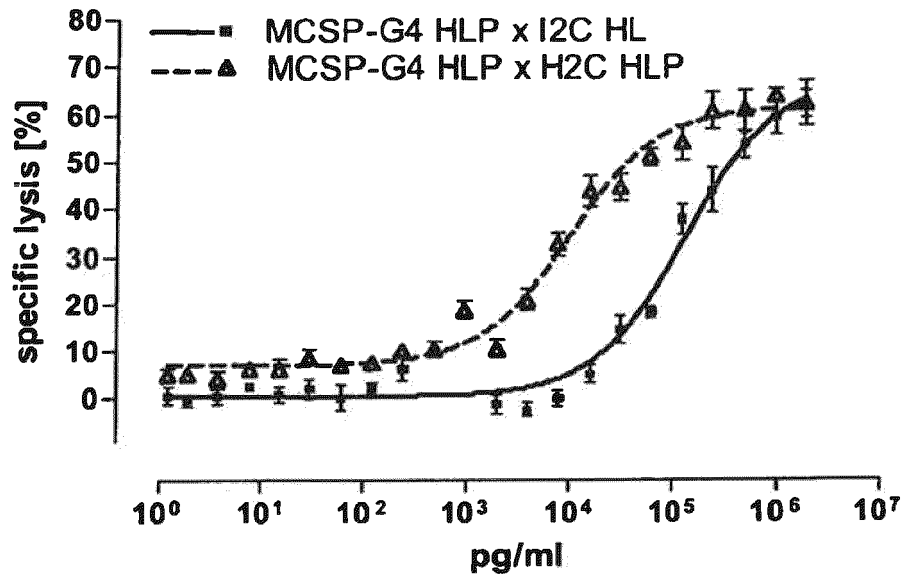


Figure 17

A)

Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human MCSP D3



B)

Effector cells: macaque T cell line 4119 LnPx

Target cells: CHO transfected with cynomolgus MCSP D3

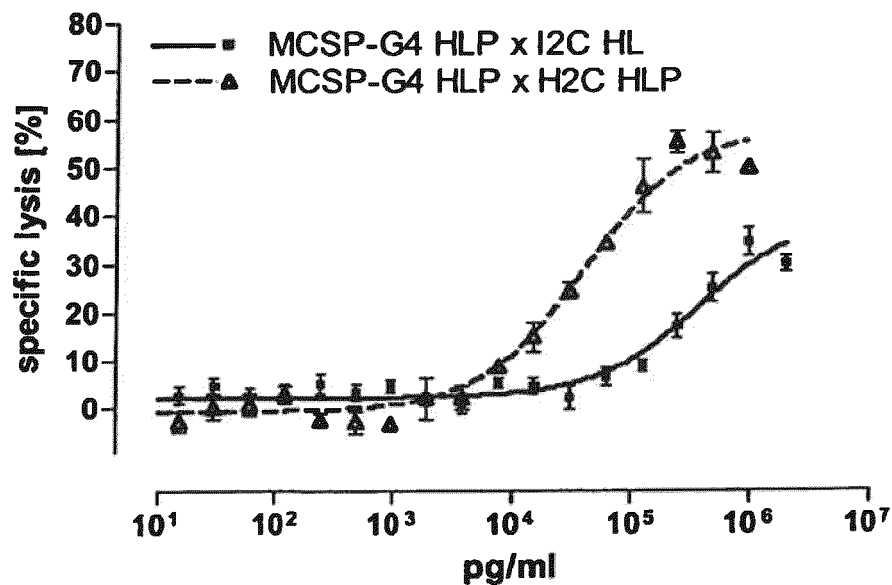


Figure 18 (1)

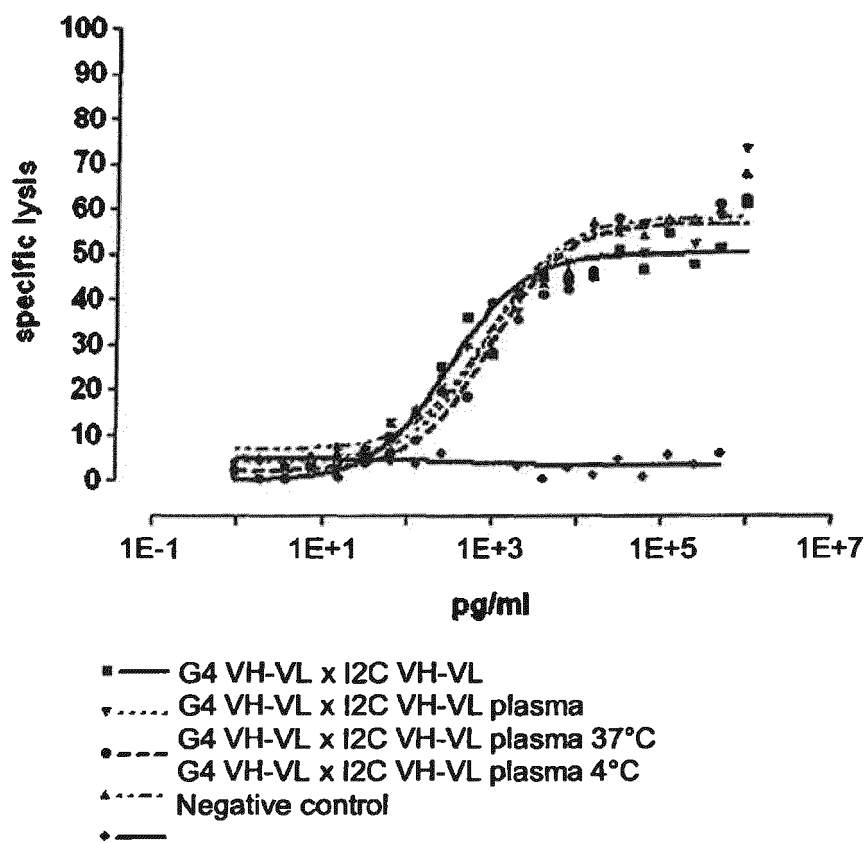


Figure 18 (2)

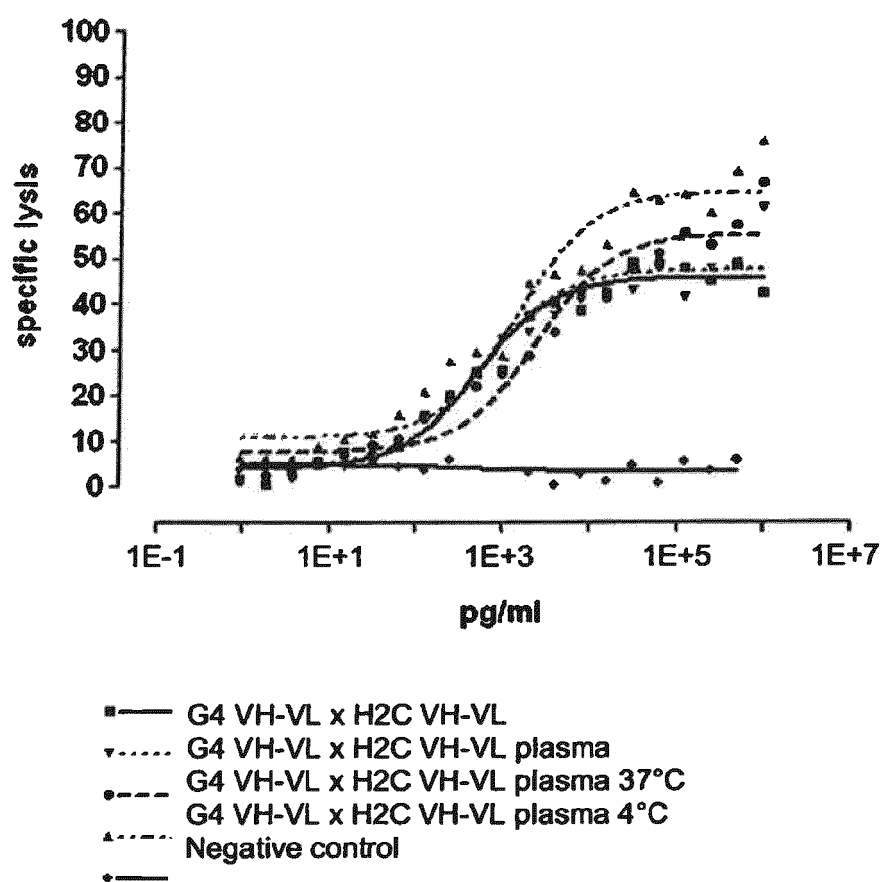


Figure 18 (3)

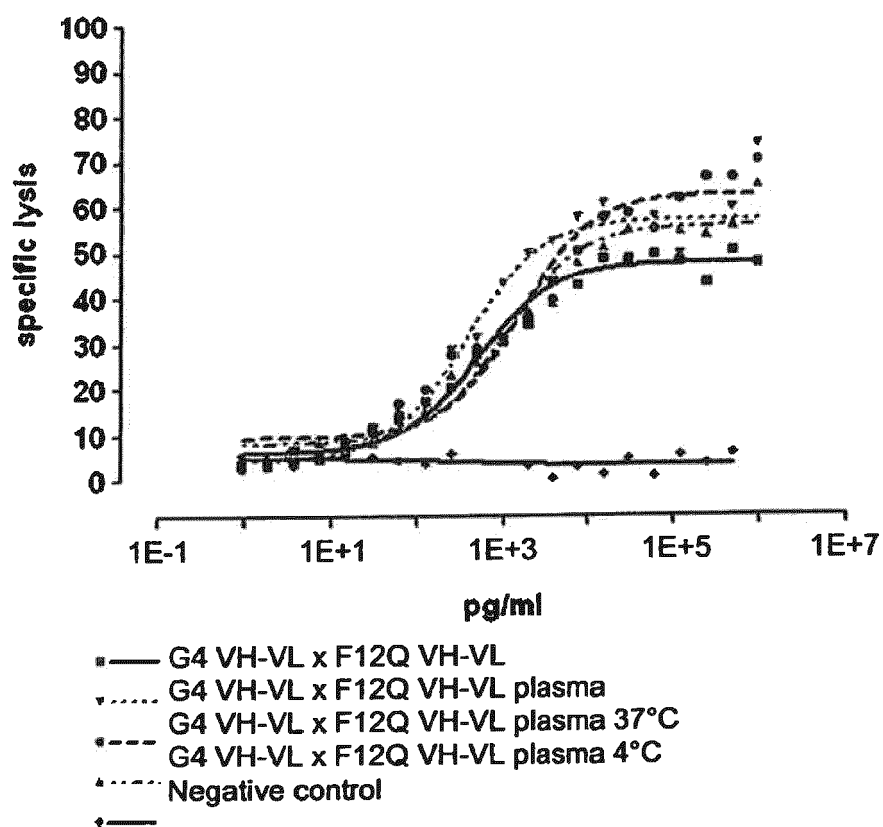


Figure 19a

Pat. 1 (0.5 $\mu\text{g}/\text{m}^2/24\text{h}$ CD19xCD3)

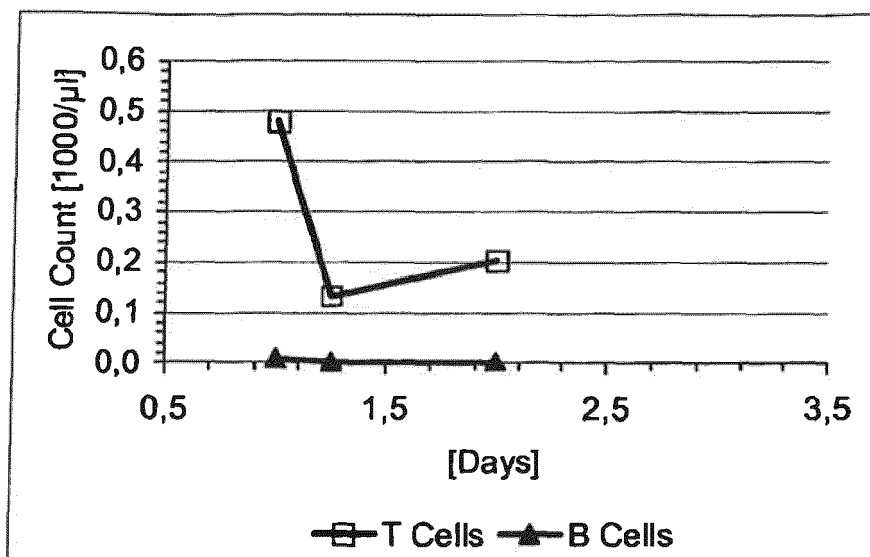


Figure 19b

Pat. 7 (1.5 $\mu\text{g}/\text{m}^2/24\text{h}$ CD19xCD3)

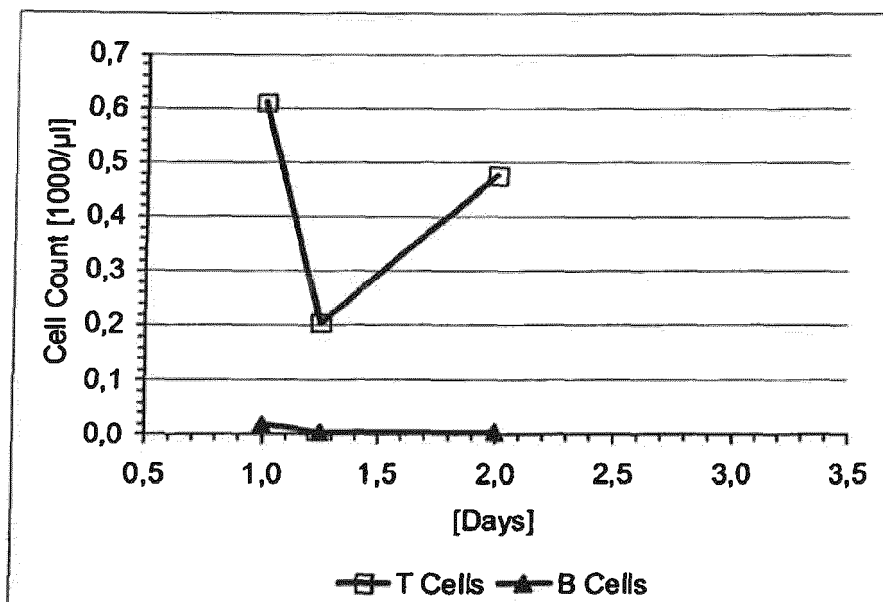


Figure 19c

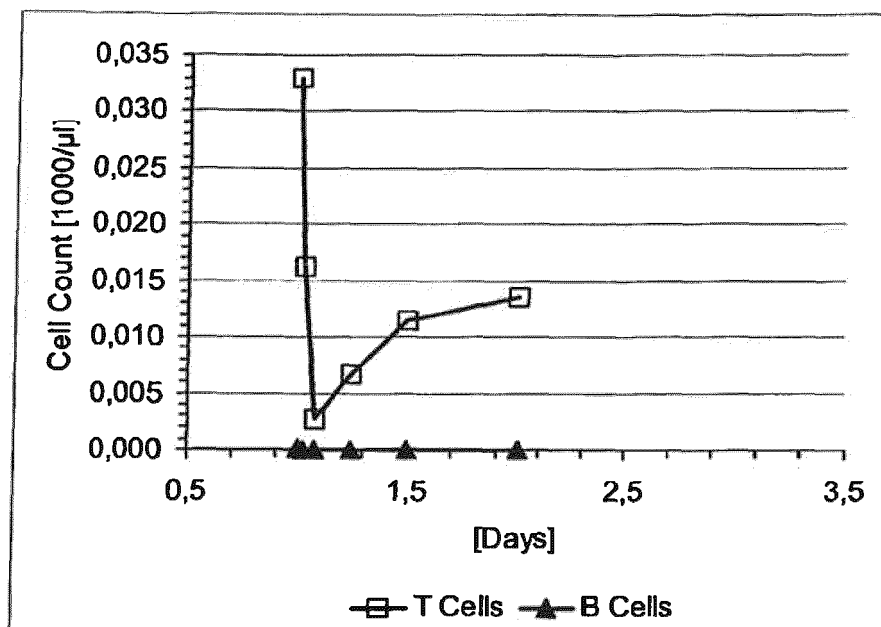
Pat. 23 ($15 \mu\text{g}/\text{m}^2/24\text{h}$ CD19xCD3)

Figure 19d

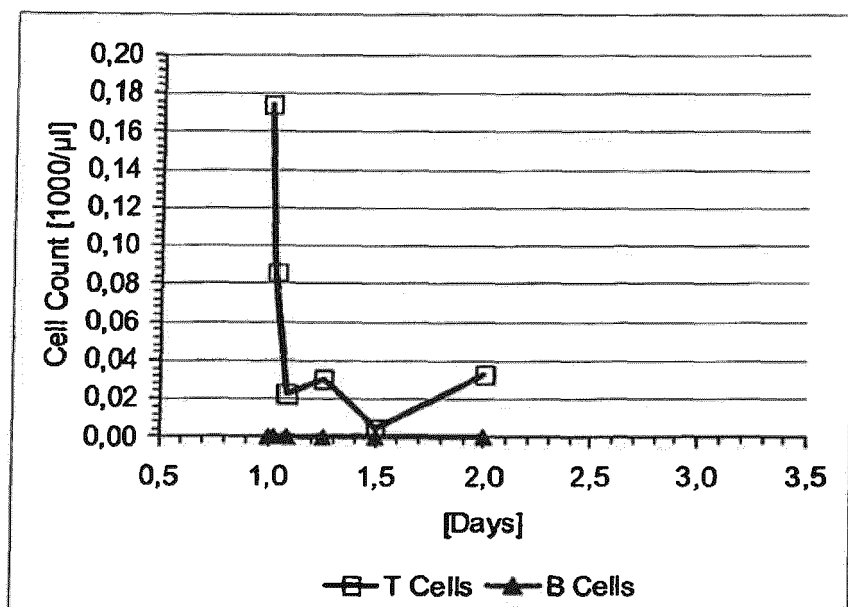
Pat. 30 ($30 \mu\text{g}/\text{m}^2/24\text{h}$ CD19xCD3)

Figure 19e

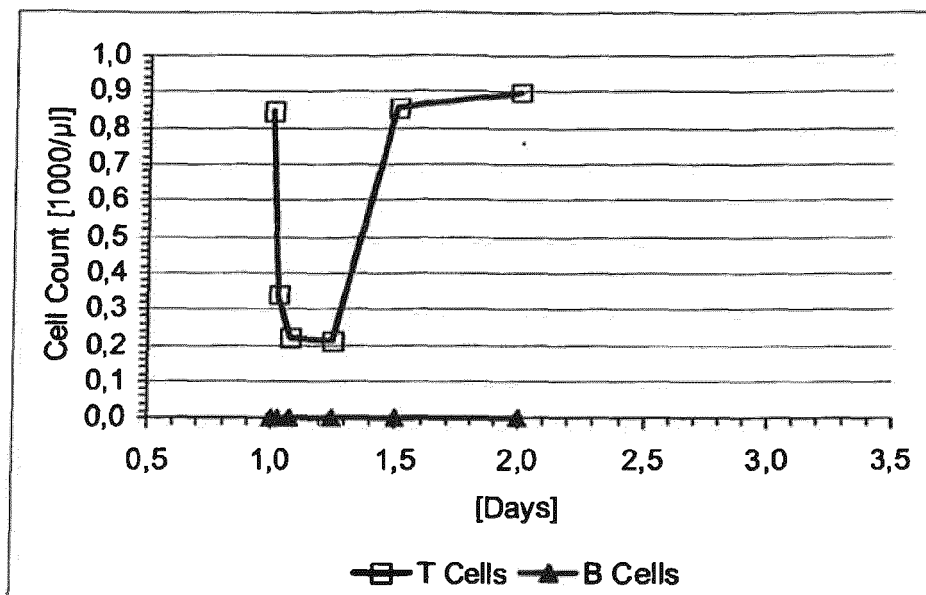
Pat. 31 ($30 \mu\text{g}/\text{m}^2/24\text{h}$ CD19xCD3)

Figure 19f

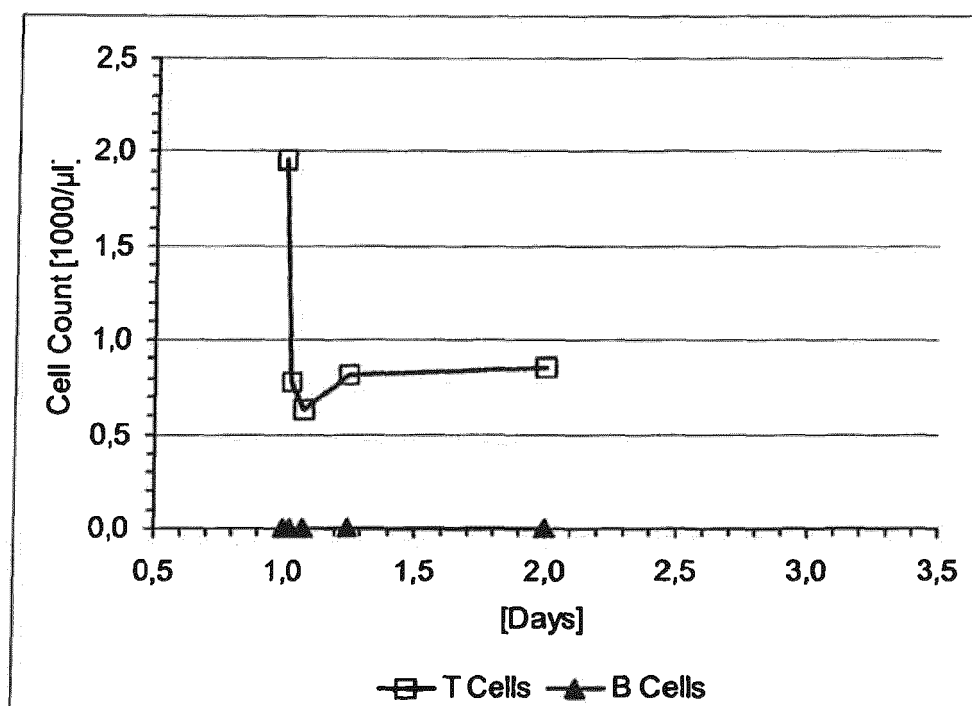
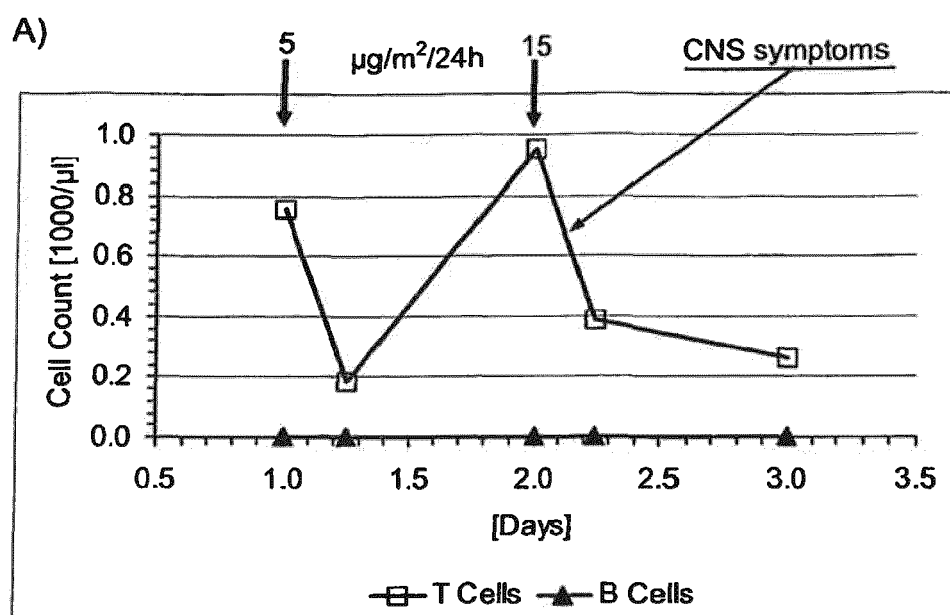
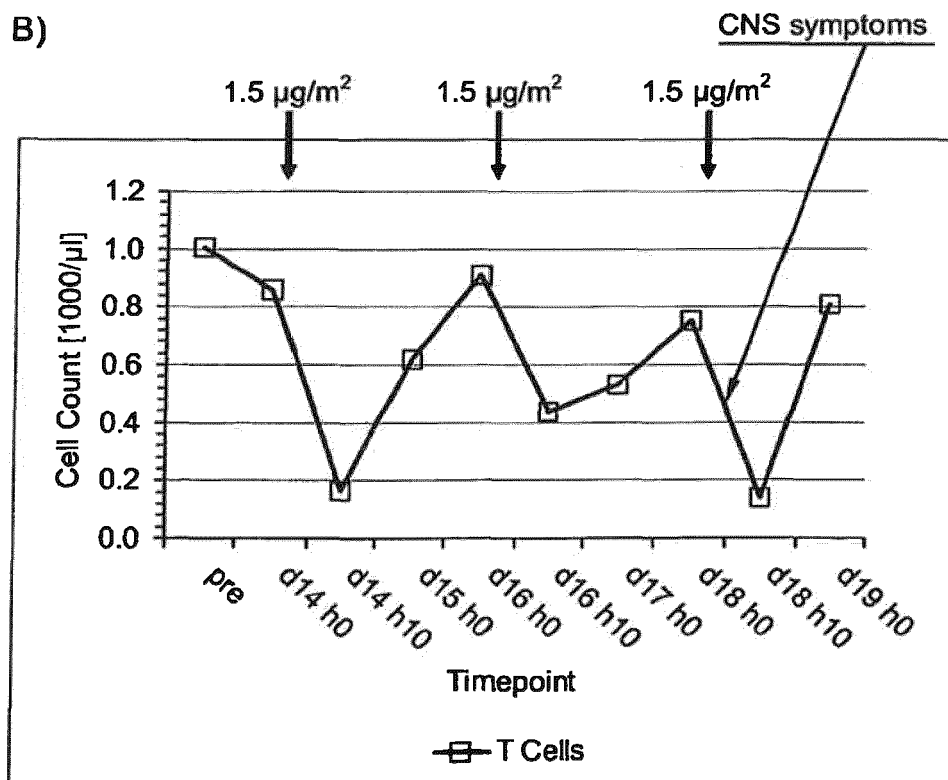
Pat. 33 ($60 \mu\text{g}/\text{m}^2/24\text{h}$ CD19xCD3)

Figure 20



Pat. 19 (continuous infusion: 5 μ g/m²/24h for 1 day followed by 15 μ g/m²/24h CD19xCD3 maintenance)



Pat. 003002 (bolus infusion trial)

Figure 21

Pat. 20 (15 $\mu\text{g}/\text{m}^2/24\text{h}$ CD19xCD3)
Ramp initiation

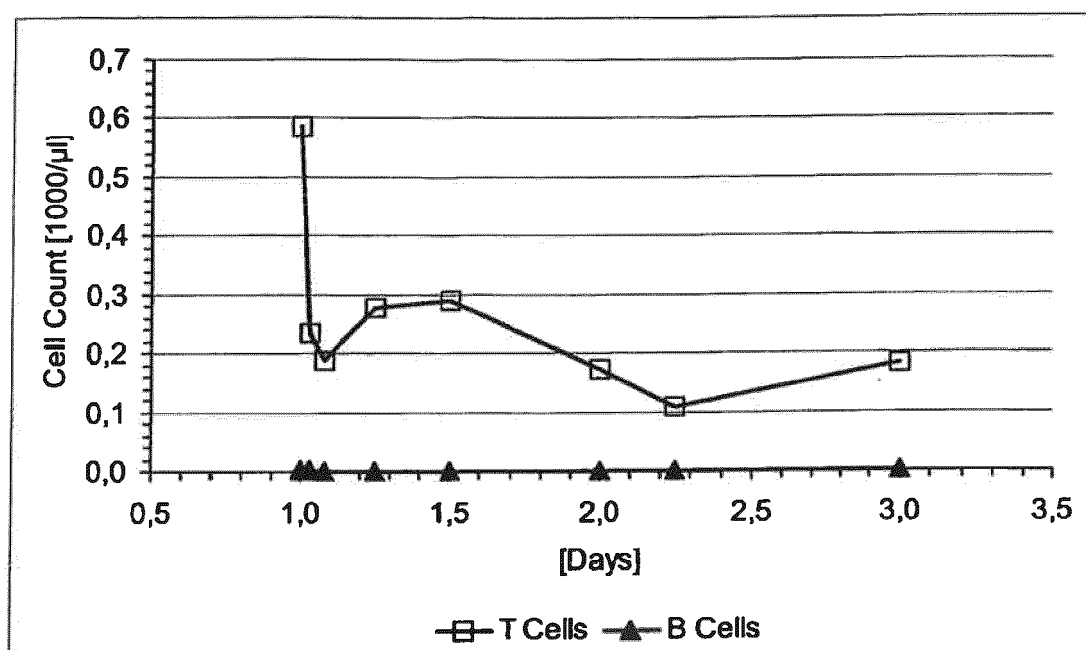


Figure 22

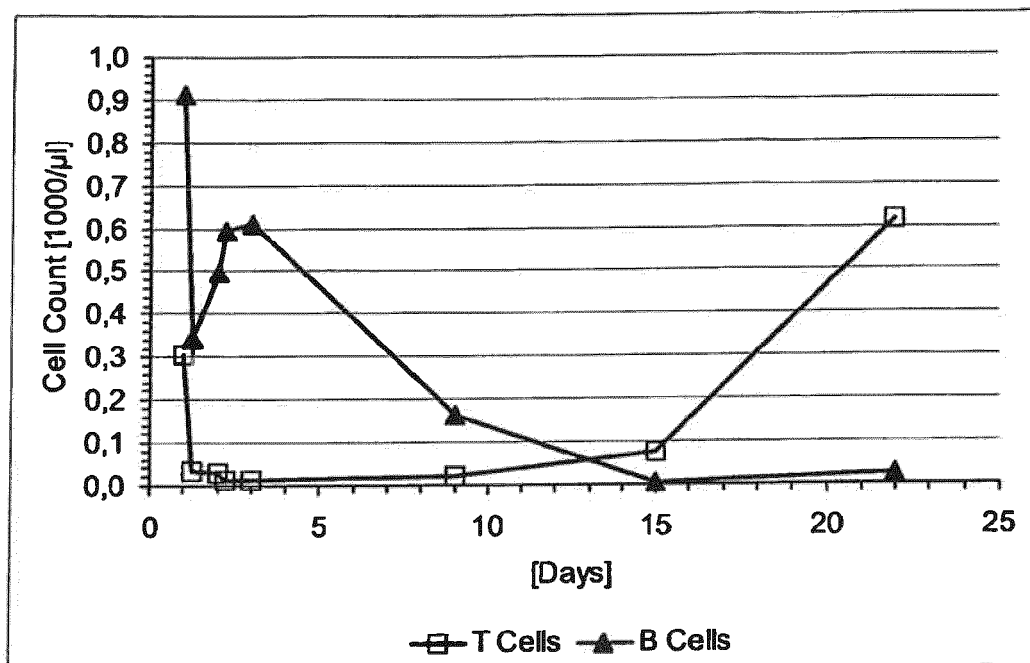
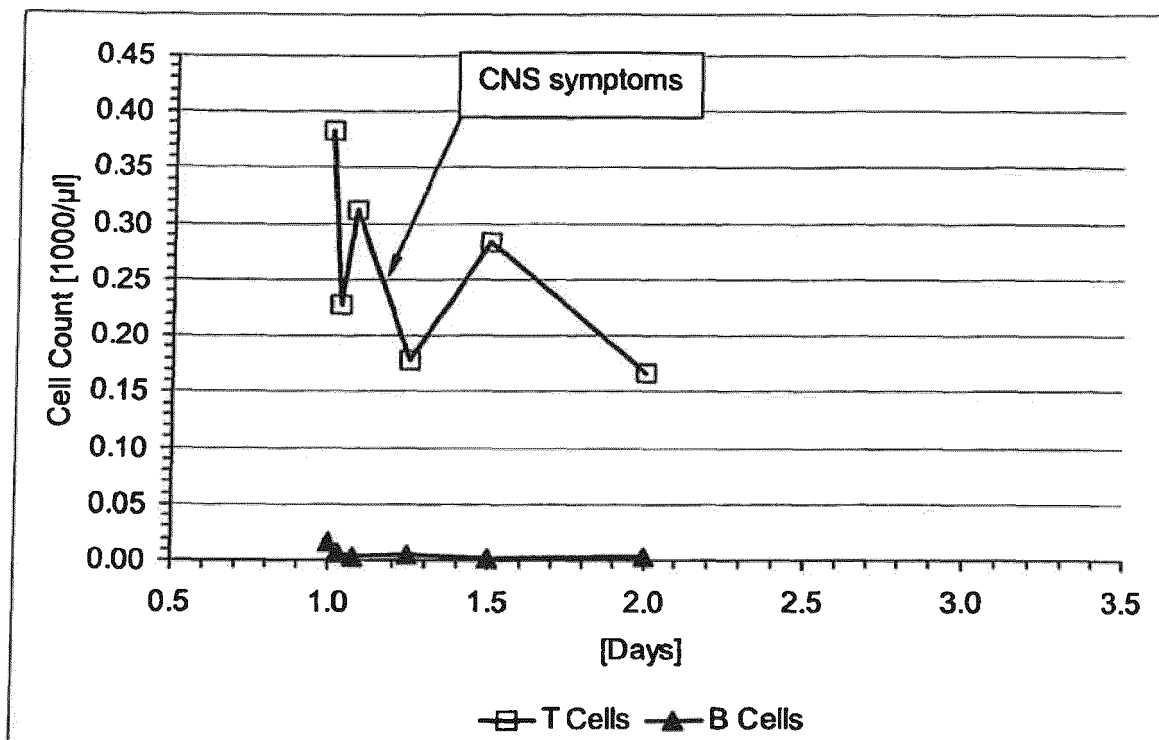
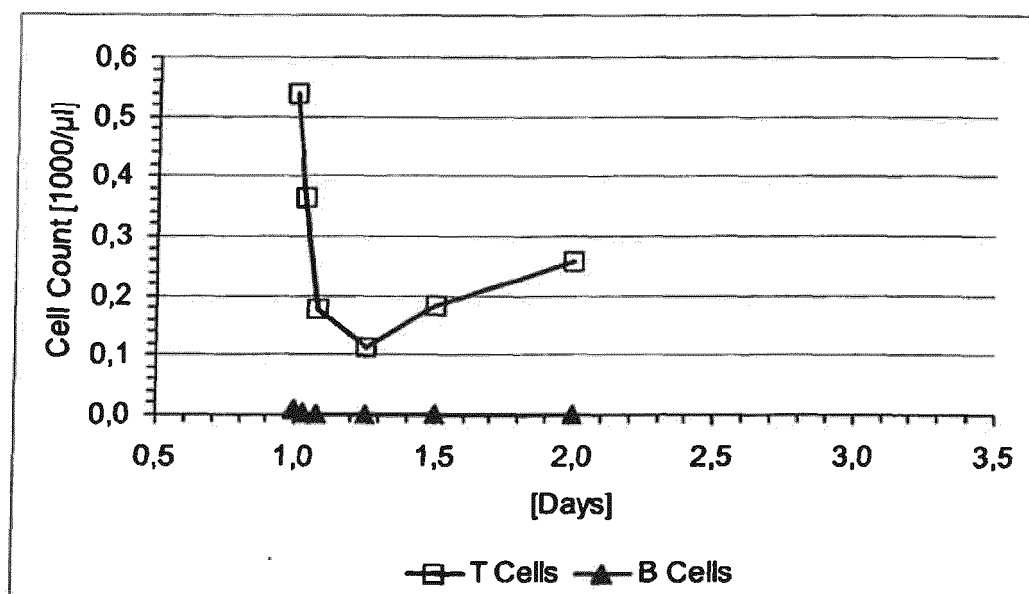
Pat. 13 (15 $\mu\text{g}/\text{m}^2/24\text{h}$ CD19xCD3)

Figure 23

Pat. 24 (15 $\mu\text{g}/\text{m}^2/24\text{h}$ CD19xCD3 without HSA)
1st Treatment start



Pat. 24 (15 $\mu\text{g}/\text{m}^2/24\text{h}$ CD19xCD3 with HSA)
2nd Treatment start



Model of T cell adhesion to endothelial cells induced by monovalent binding to context dependent CD3 epitopes

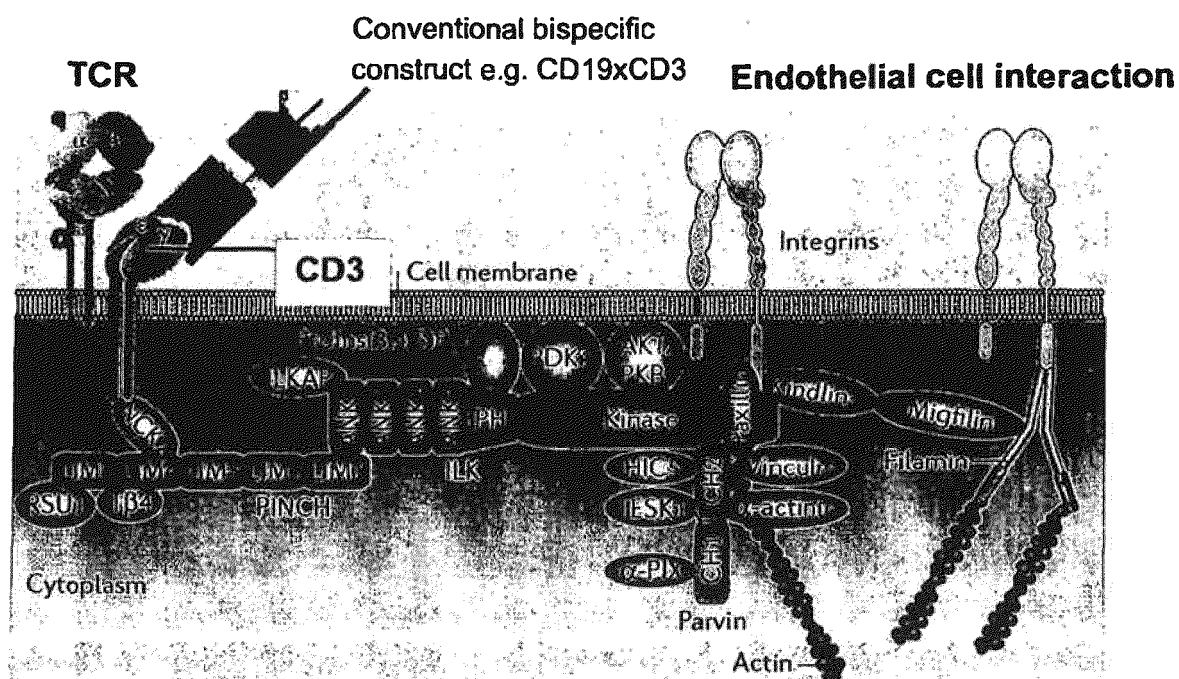


Figure 24

Figure 25

**Cytotoxic activity of cynomolgus test material
CD33-AF5 VH-VL x I2C VH-VL**

Target cells: cyno CD33 CHO; effector cells: 4119 LnPx
E:T-ratio 10:1; assay duration: 18 h
EC50: 2.7 ng/ml

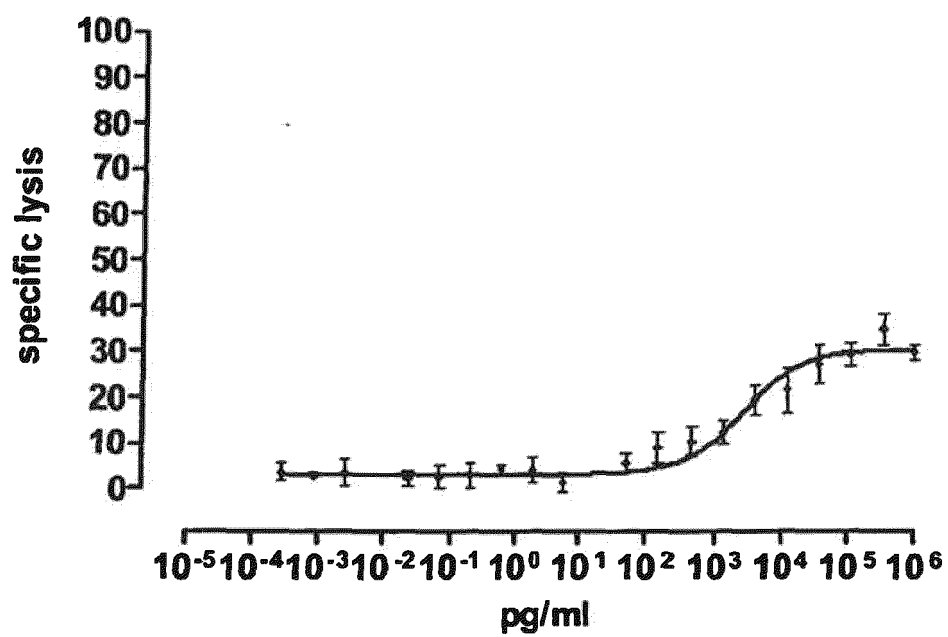


Figure 26 A

**Dose- and time-dependent depletion of blood CD33-monocytes through
CD33-AF5 VH-VL x I2C VH-VL**

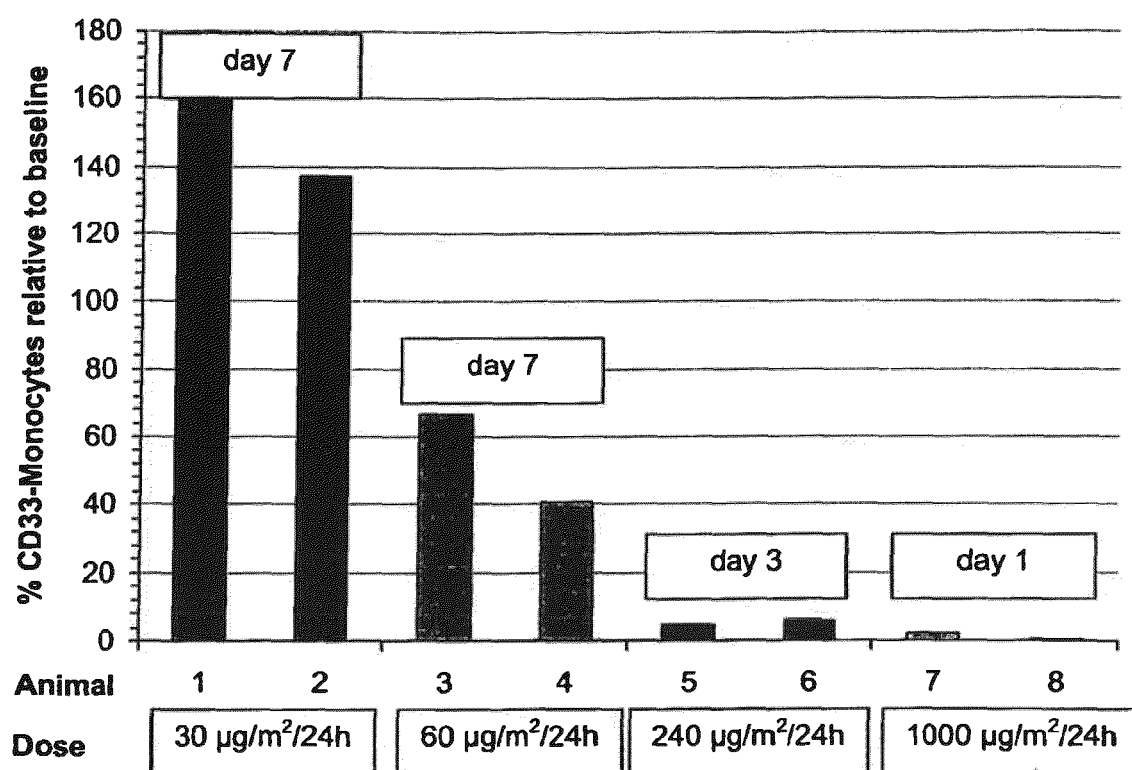


Figure 26 B (1)

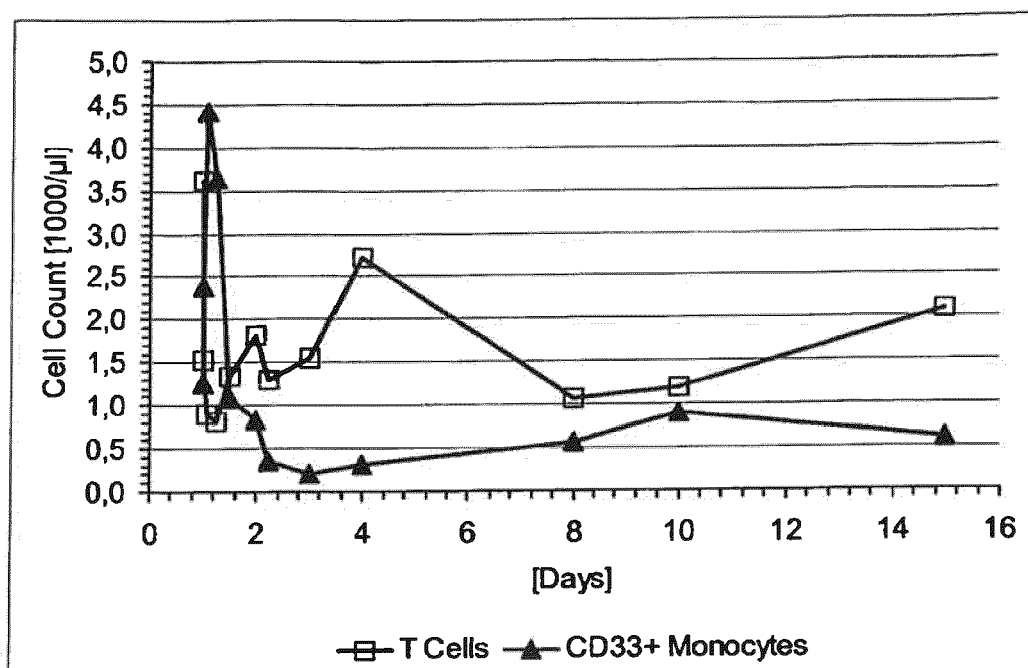
Animal 9 (120 $\mu\text{g}/\text{m}^2/24\text{h}$ CD33xCD3)

Figure 26 B (2)

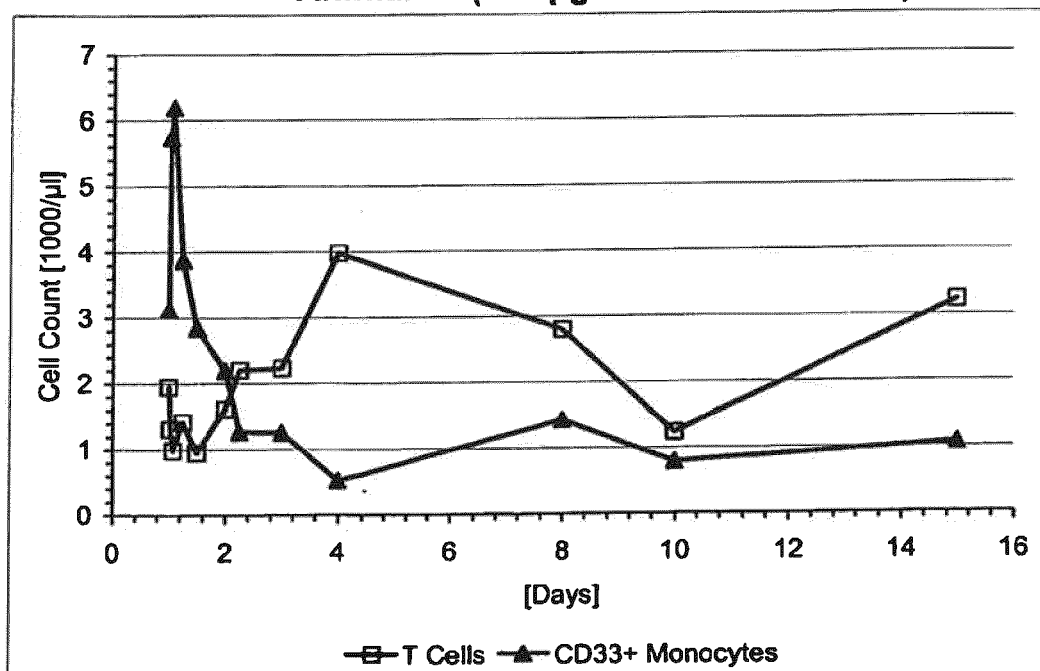
Animal 10 (120 $\mu\text{g}/\text{m}^2/24\text{h}$ CD33xCD3)

Figure 27

**Cytotoxic activity of cynomolgus test material
MCSP-G4 VH-VL x I2C VH-VL**

Target cells: cyno MCSP CHO; effector cells: 4119 LnPx
E:T-ratio 10:1; assay duration: 18 h
EC50: 1.9 ng/ml

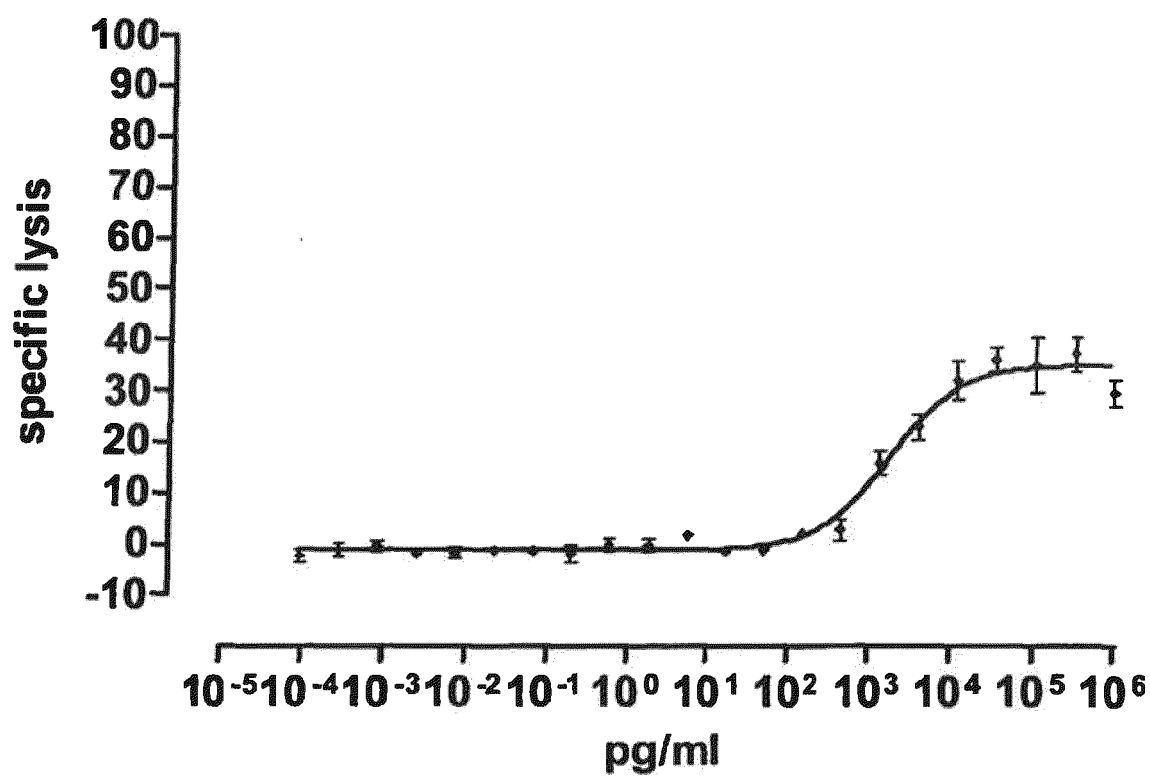


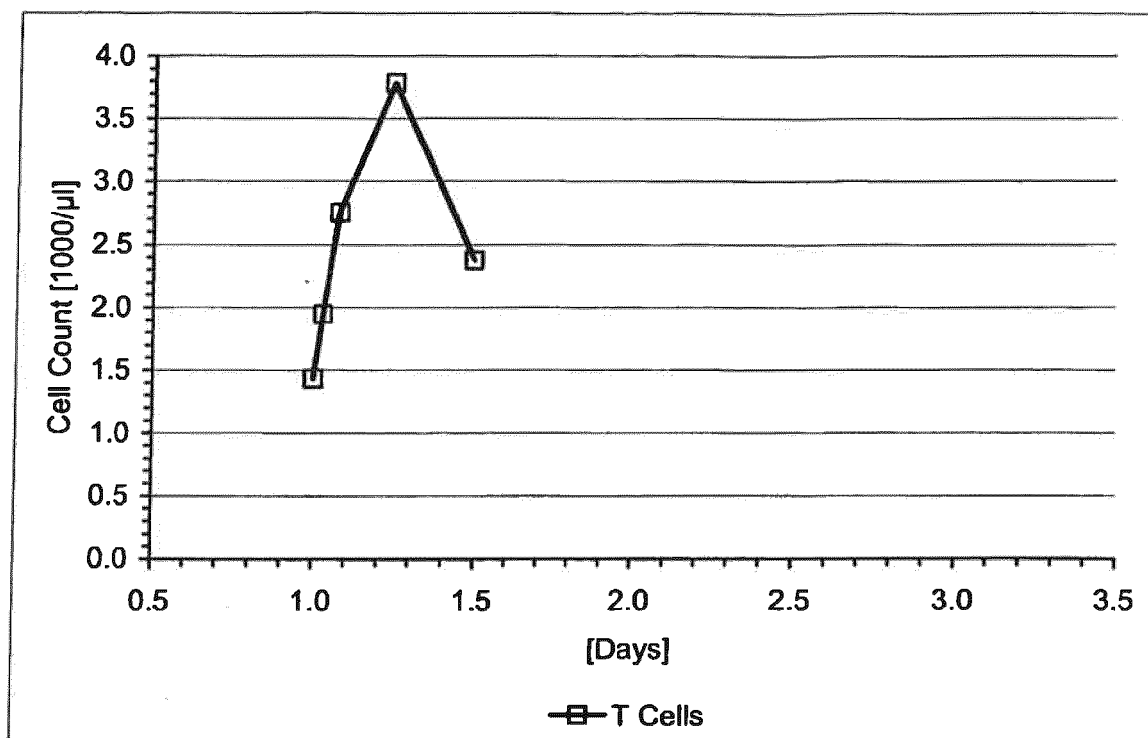
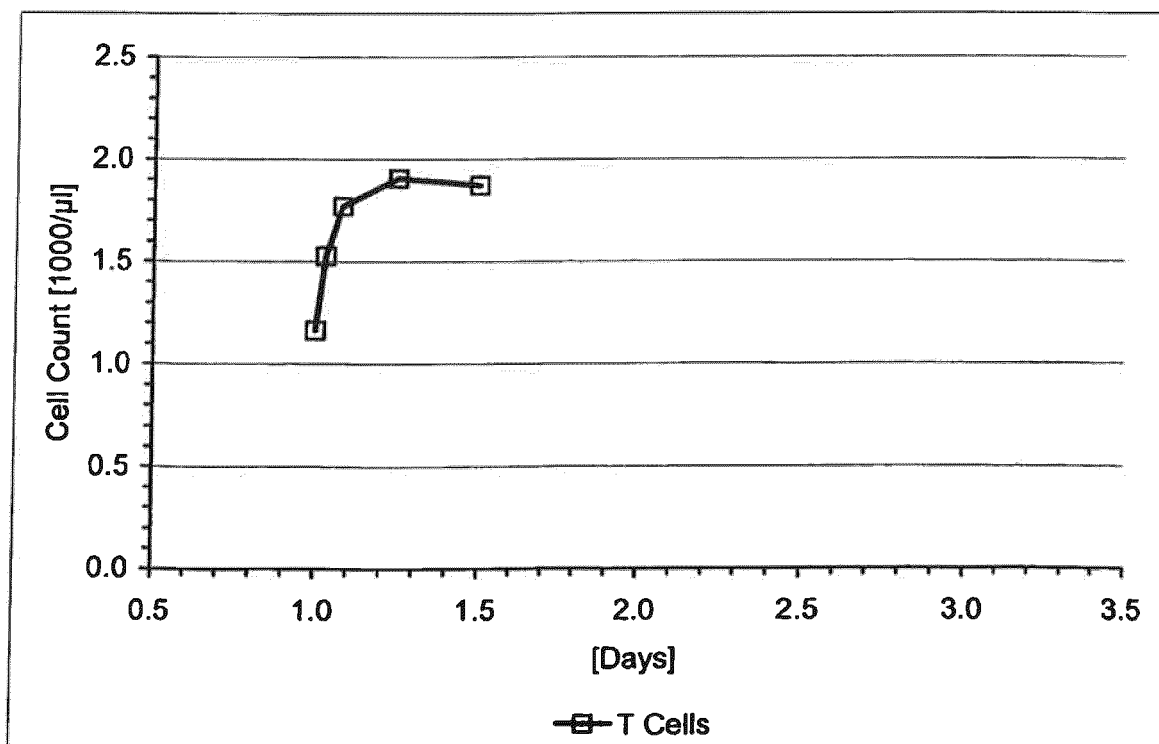
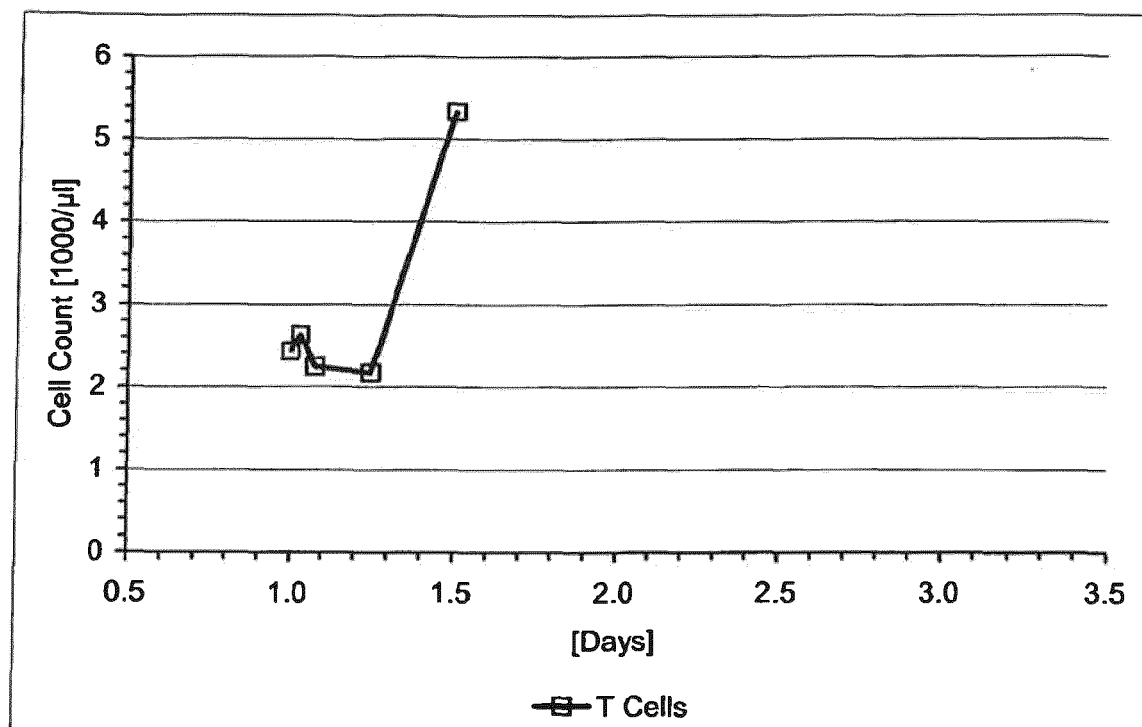
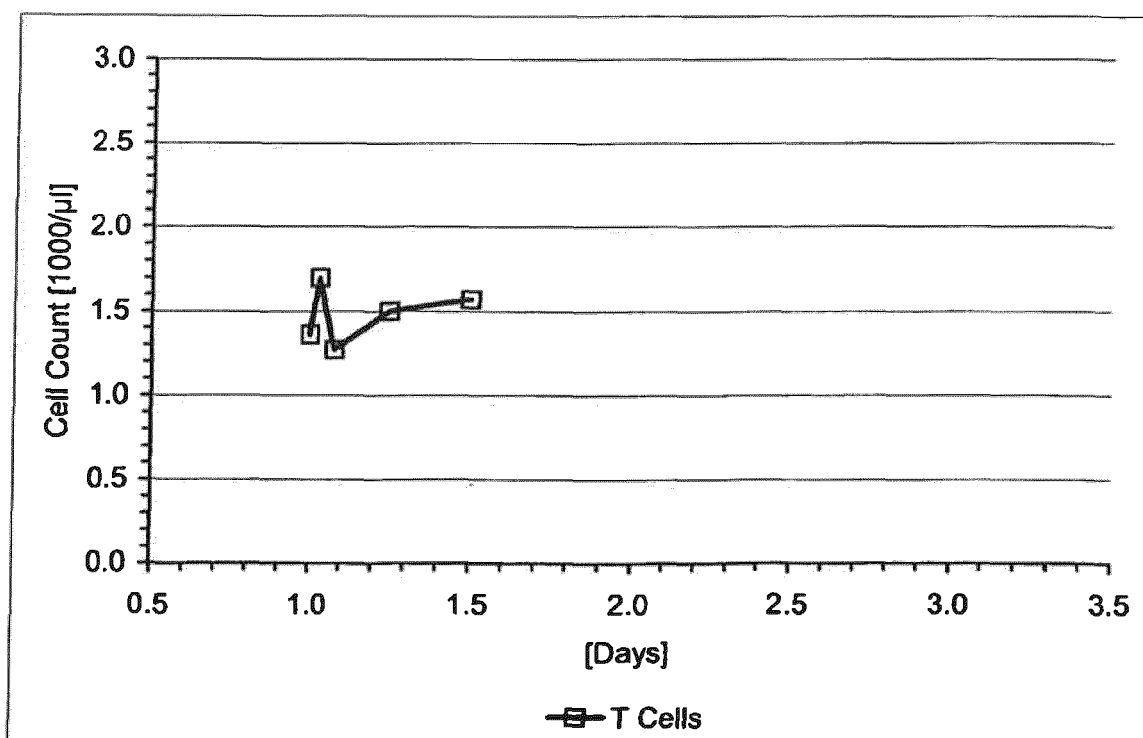
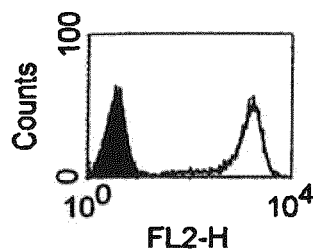
Figure 28 (1)**Animal 1 (60 $\mu\text{g}/\text{m}^2/24\text{h}$ MCSP-G4 VH-VL x I2C VH-VL)****Animal 2 (240 $\mu\text{g}/\text{m}^2/24\text{h}$ MCSP-G4 VH-VL x I2C VH-VL)**

Figure 28 (2)**Animal 3 (240 $\mu\text{g}/\text{m}^2/24\text{h}$ MCSP-G4 VH-VL x I2C VH-VL)****Animal 4 (1000 $\mu\text{g}/\text{m}^2/24\text{h}$ MCSP-G4 VH-VL x I2C VH-VL)**

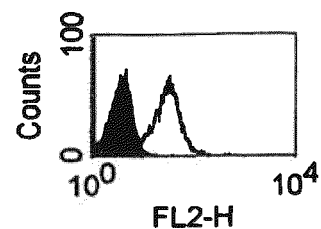
Human CD33 transfected CHO

AH11HLxF12QHL



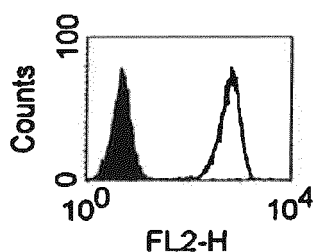
HPB-ALL

AH11HLxF12QHL



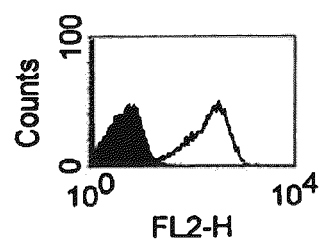
Macaque CD33 transfected CHO

AH11HLxF12QHL



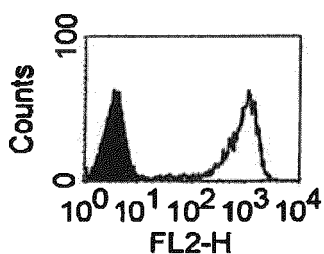
Macaque PBMC

AH11HLxF12QHL



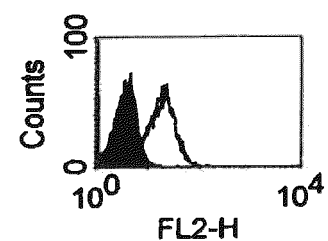
Human CD33 transfected CHO

AH11HLxH2CHL



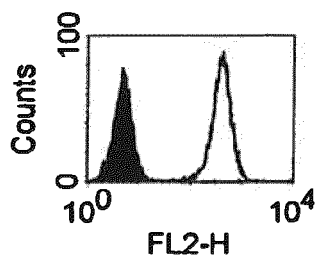
HPB-ALL

AH11HLxH2CHL



Macaque CD33 transfected CHO

AH11HLxH2CHL



Macaque PBMC

AH11HLxH2CHL

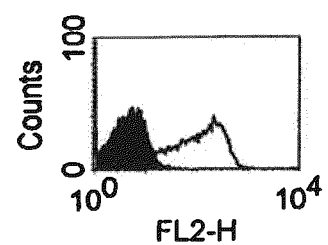


Figure 29(1)

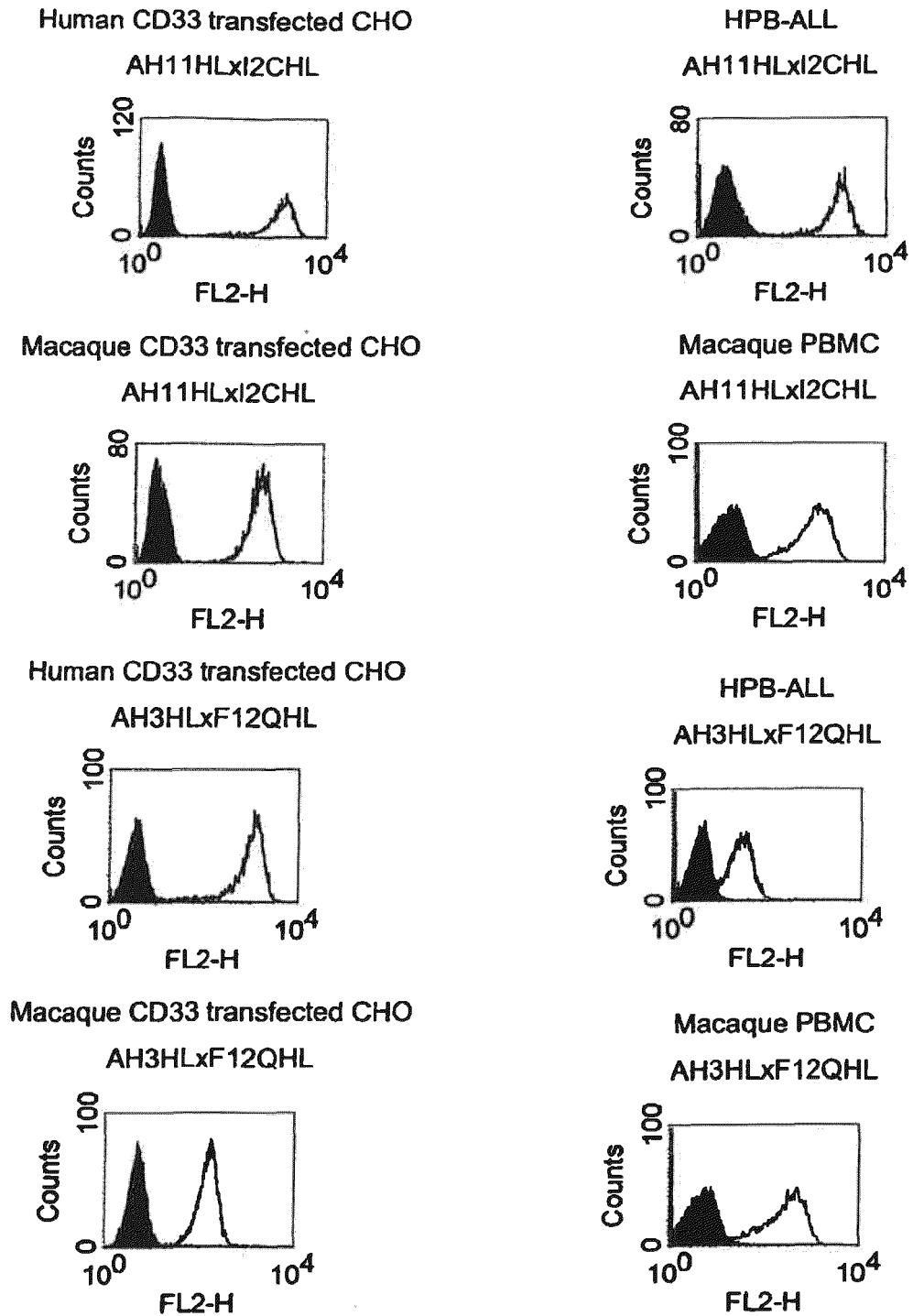


Figure 29(2)

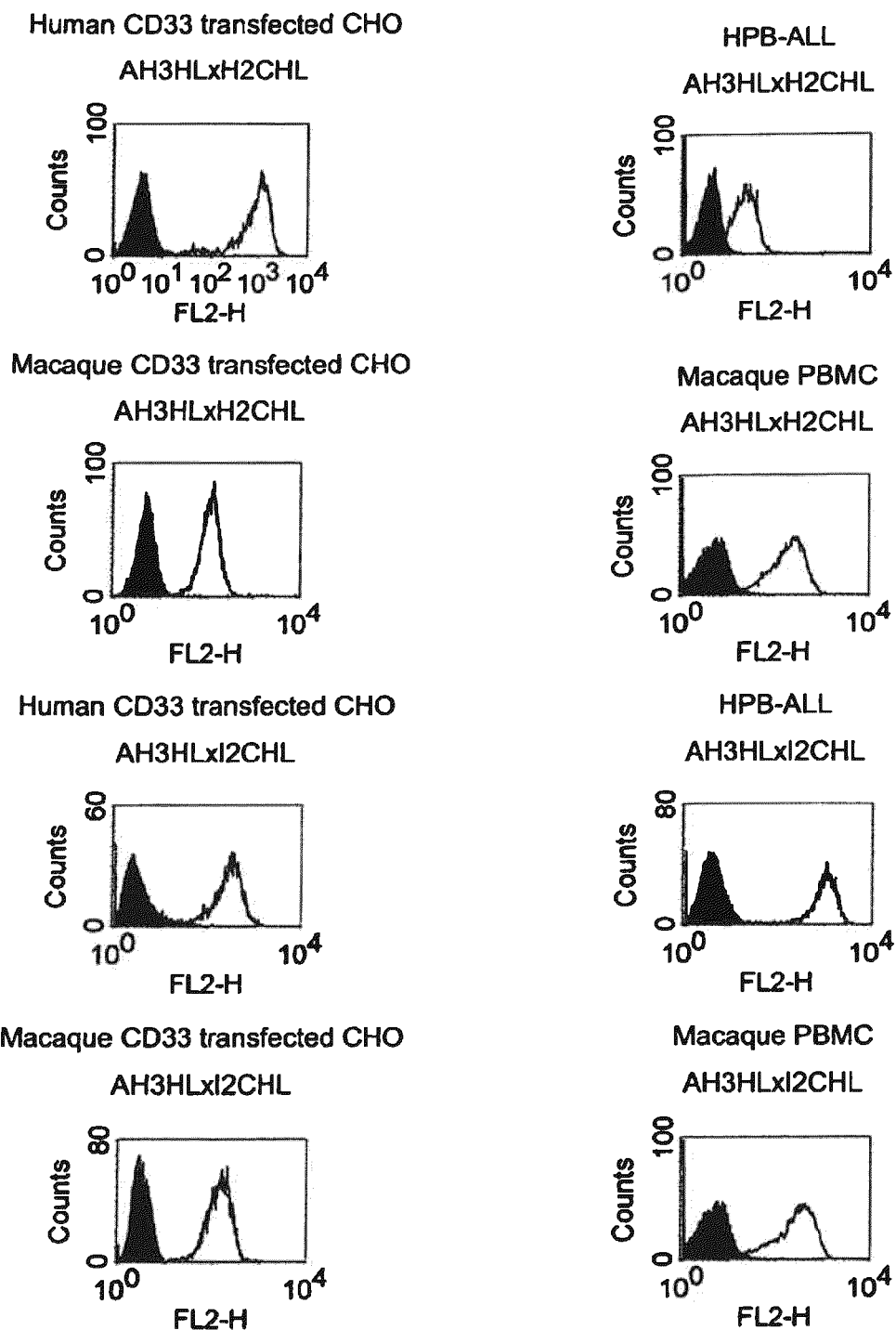


Figure 29(3)

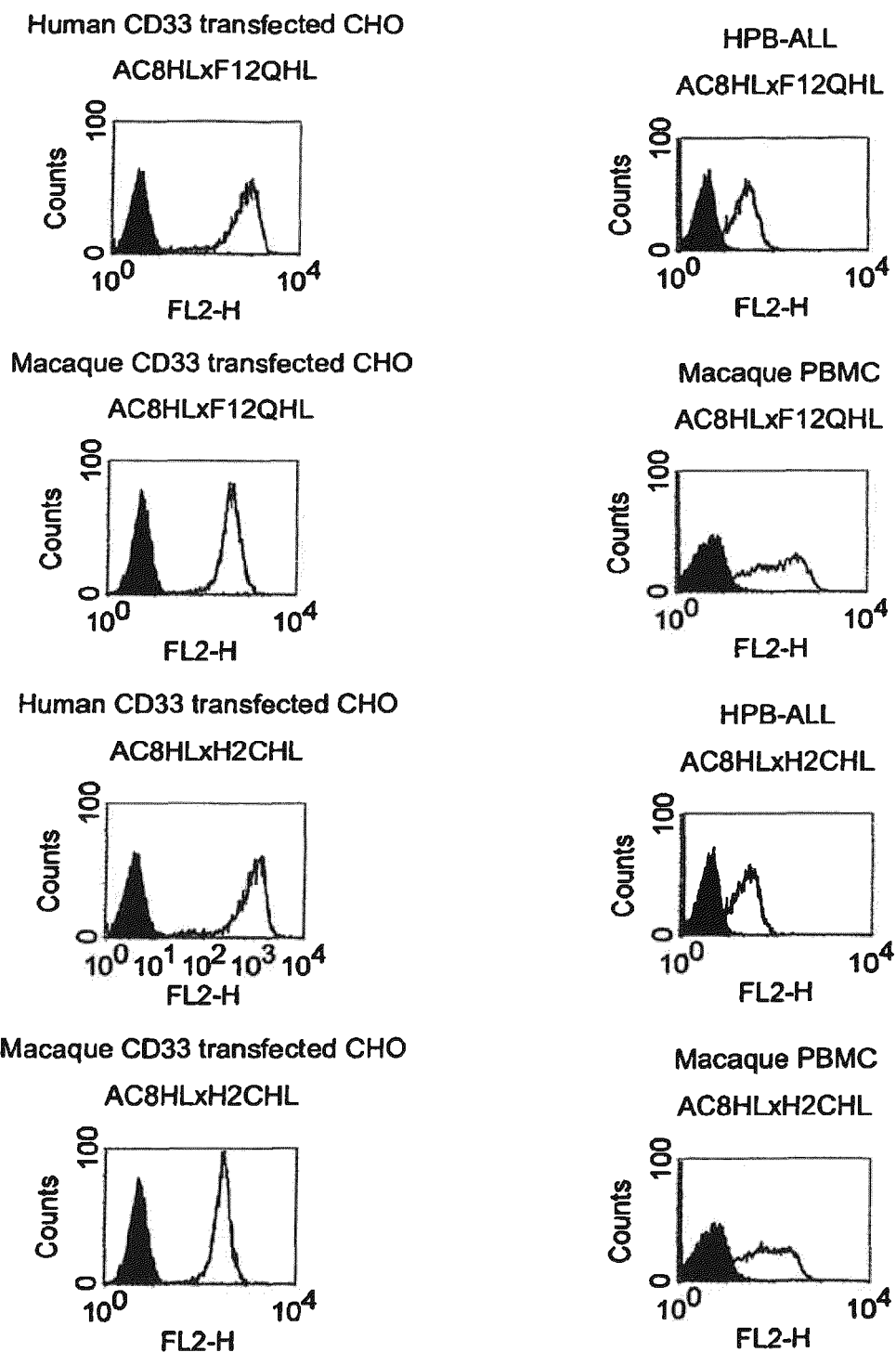
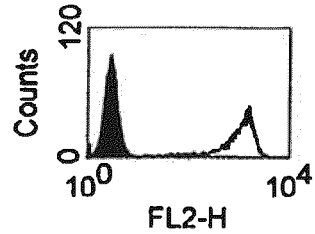


Figure 29(4)

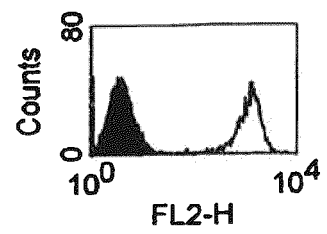
Human CD33 transfected CHO

AC8HLxI2CHL



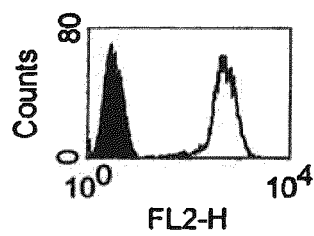
HPB-ALL

AC8HLxI2CHL



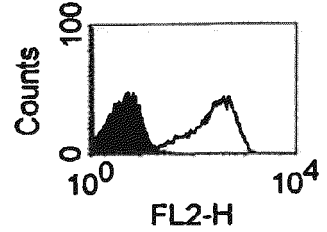
Macaque CD33 transfected CHO

AC8HLxI2CHL



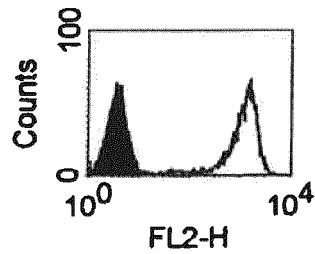
Macaque PBMC

AC8HLxI2CHL



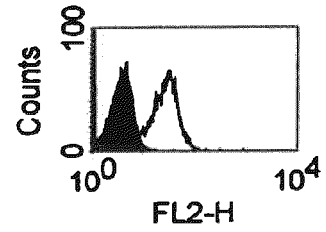
Human CD33 transfected CHO

AF5HLxF12QHL



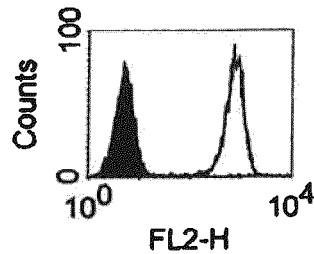
HPB-ALL

AF5HLxF12QHL



Macaque CD33 transfected CHO

AF5HLxF12QHL



Macaque PBMC

AF5HLxF12QHL

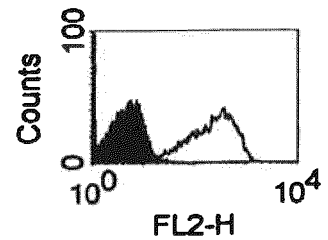


Figure 29(5)

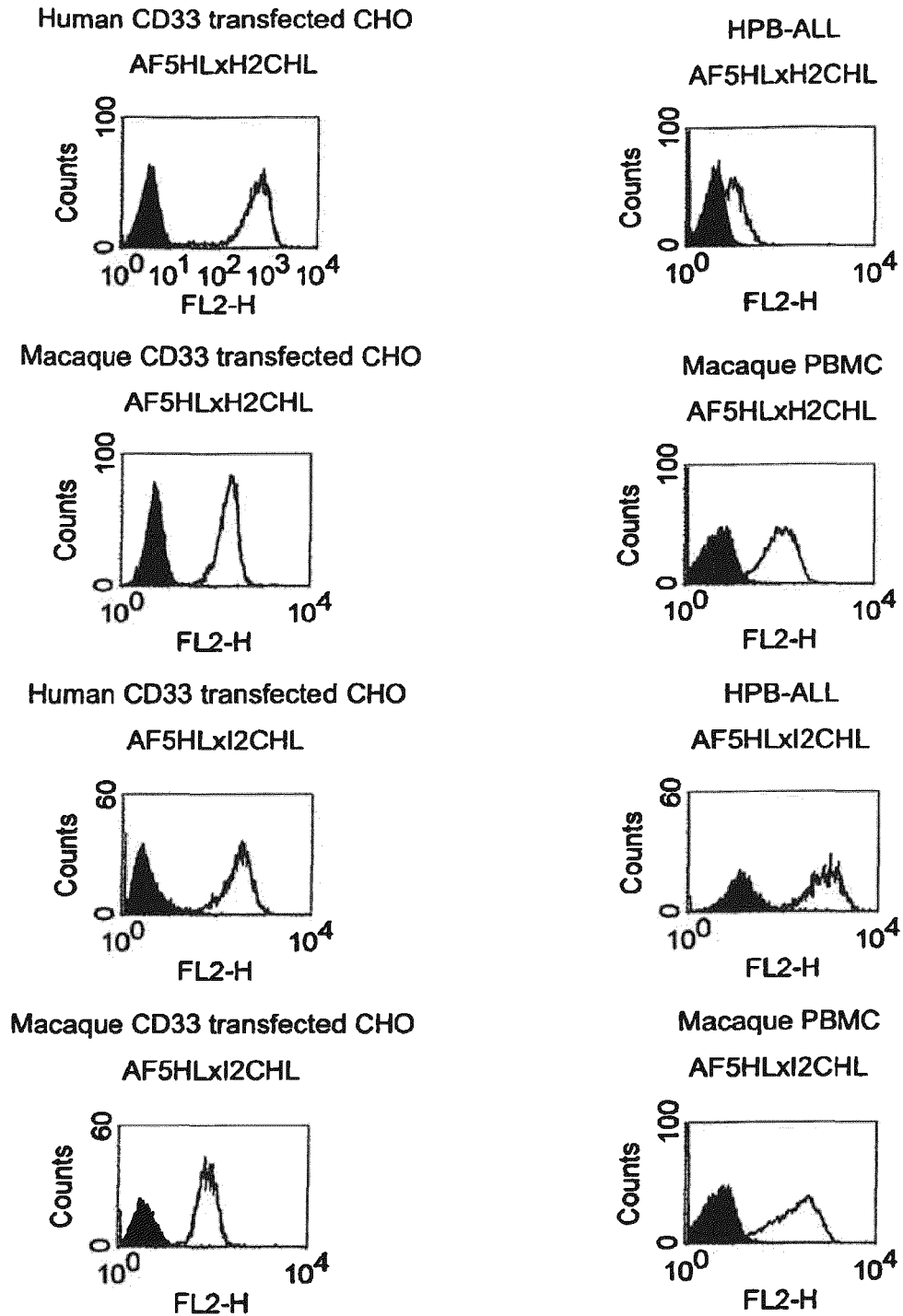


Figure 29(6)

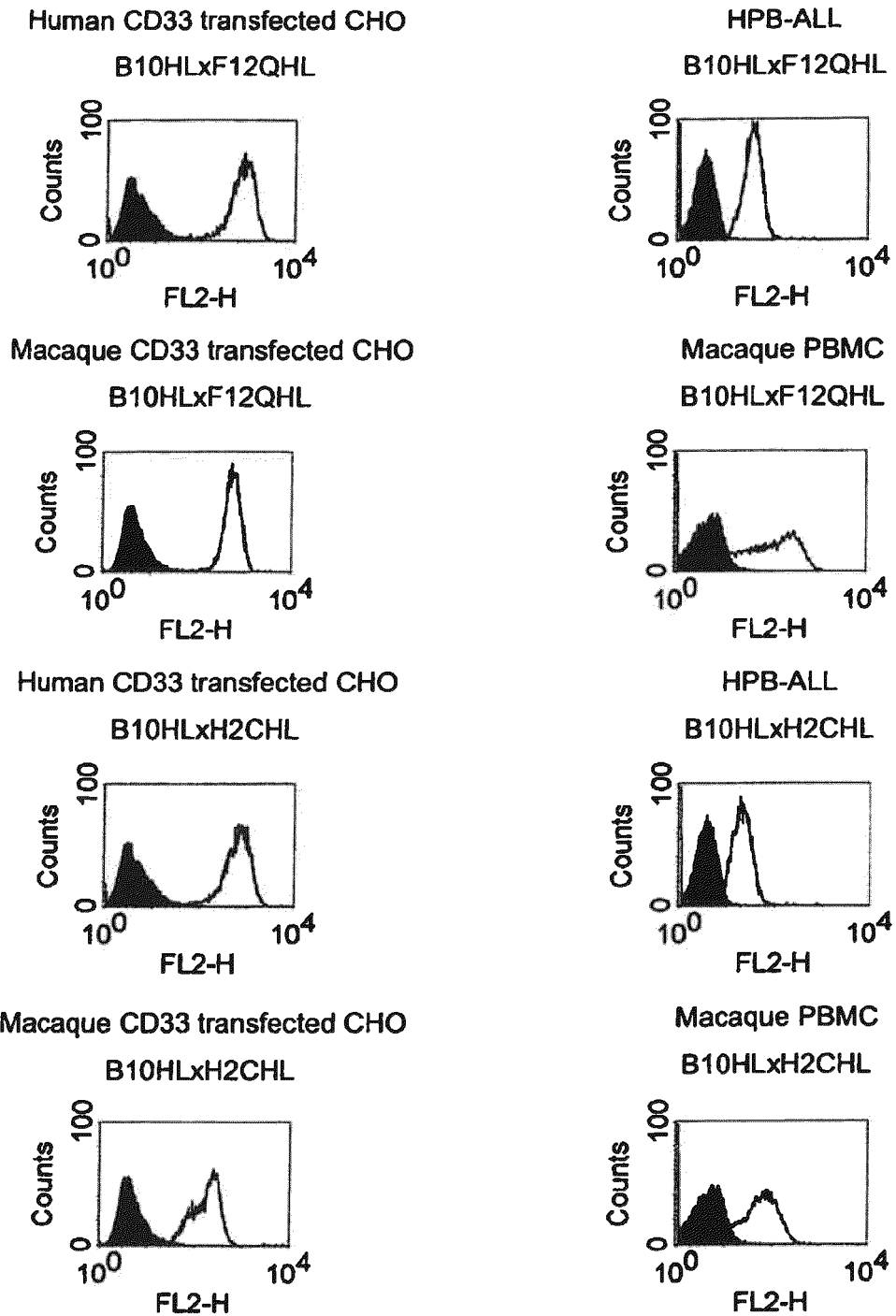


Figure 29(7)

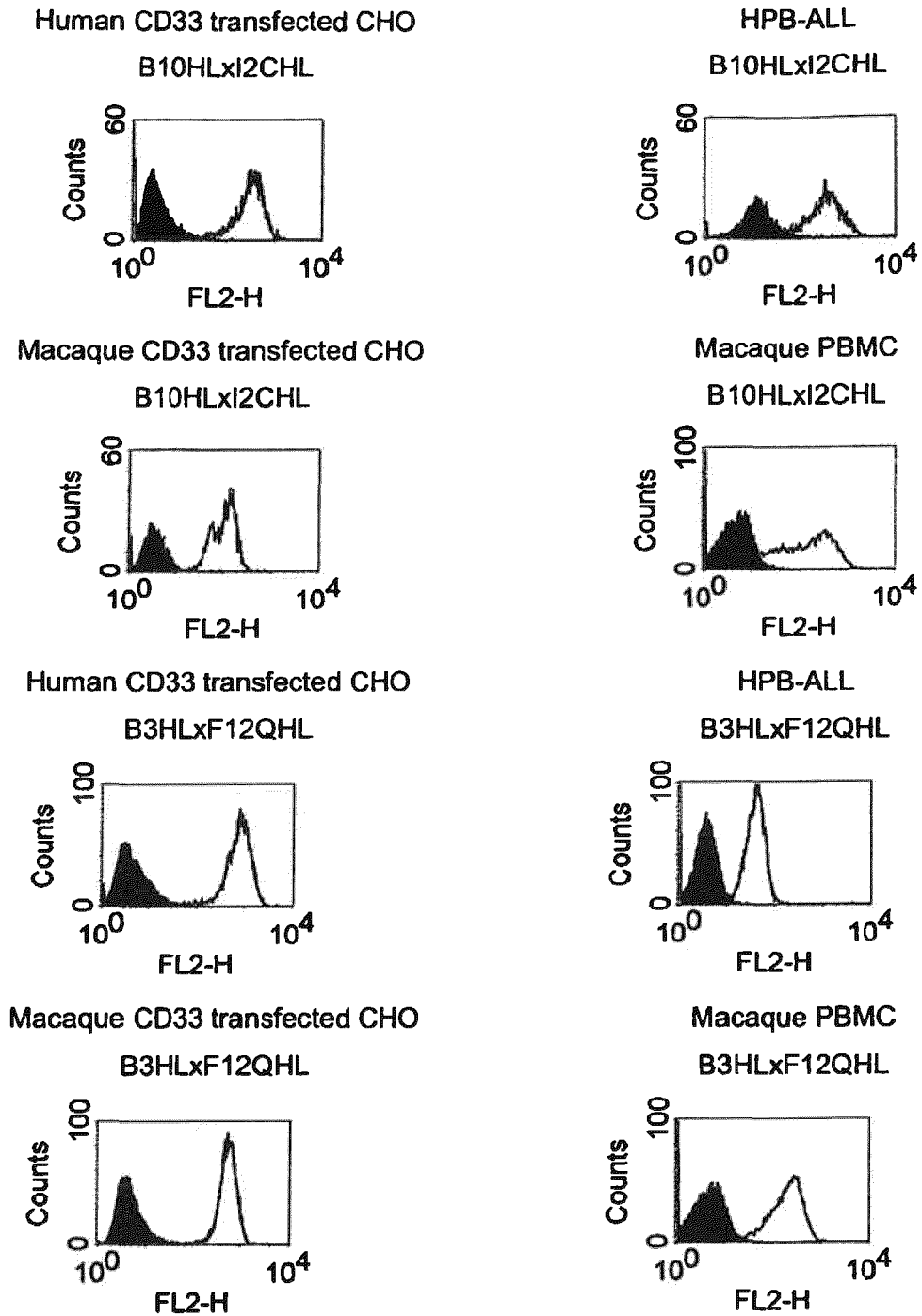


Figure 29(8)

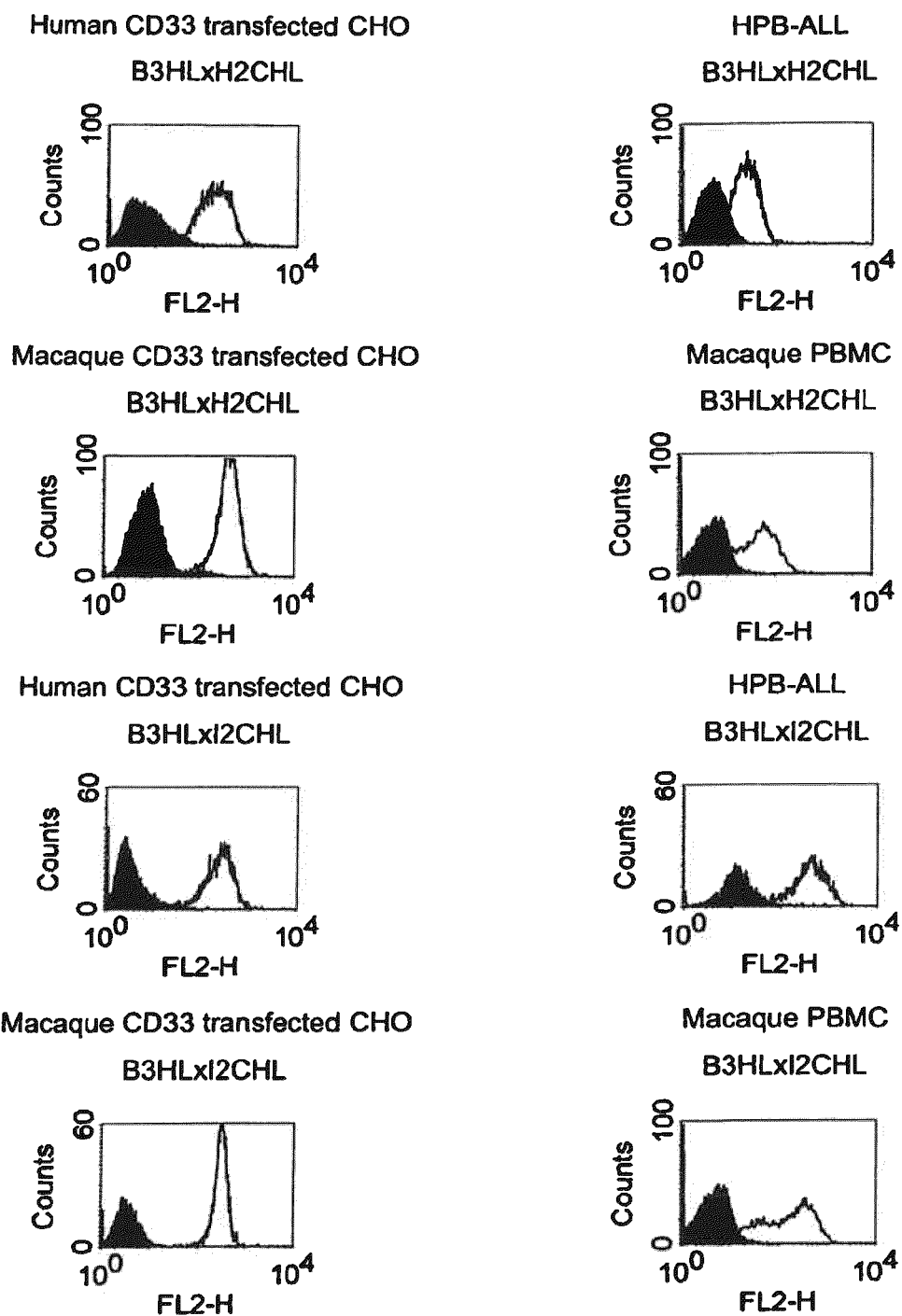


Figure 29(9)

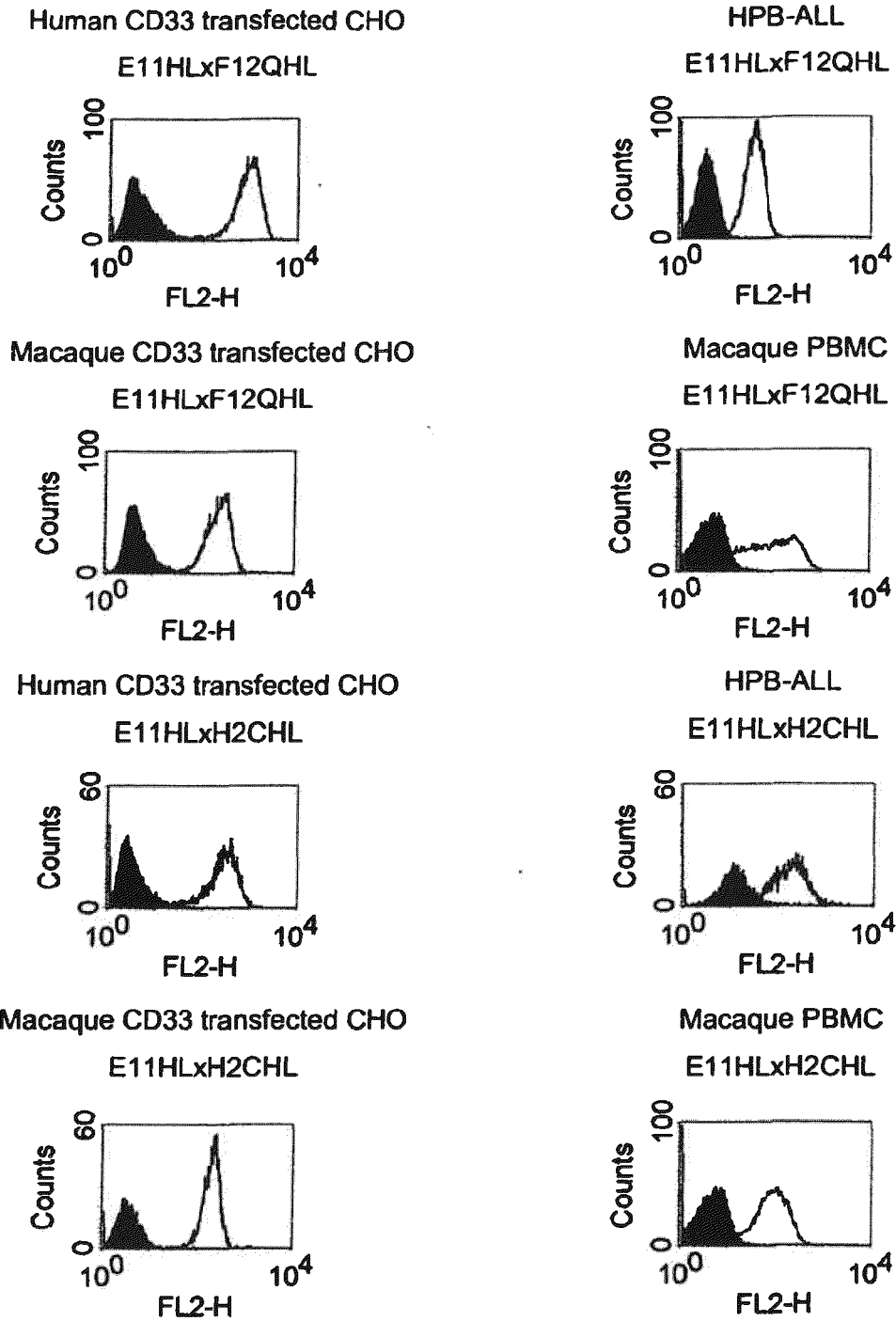


Figure 29(10)

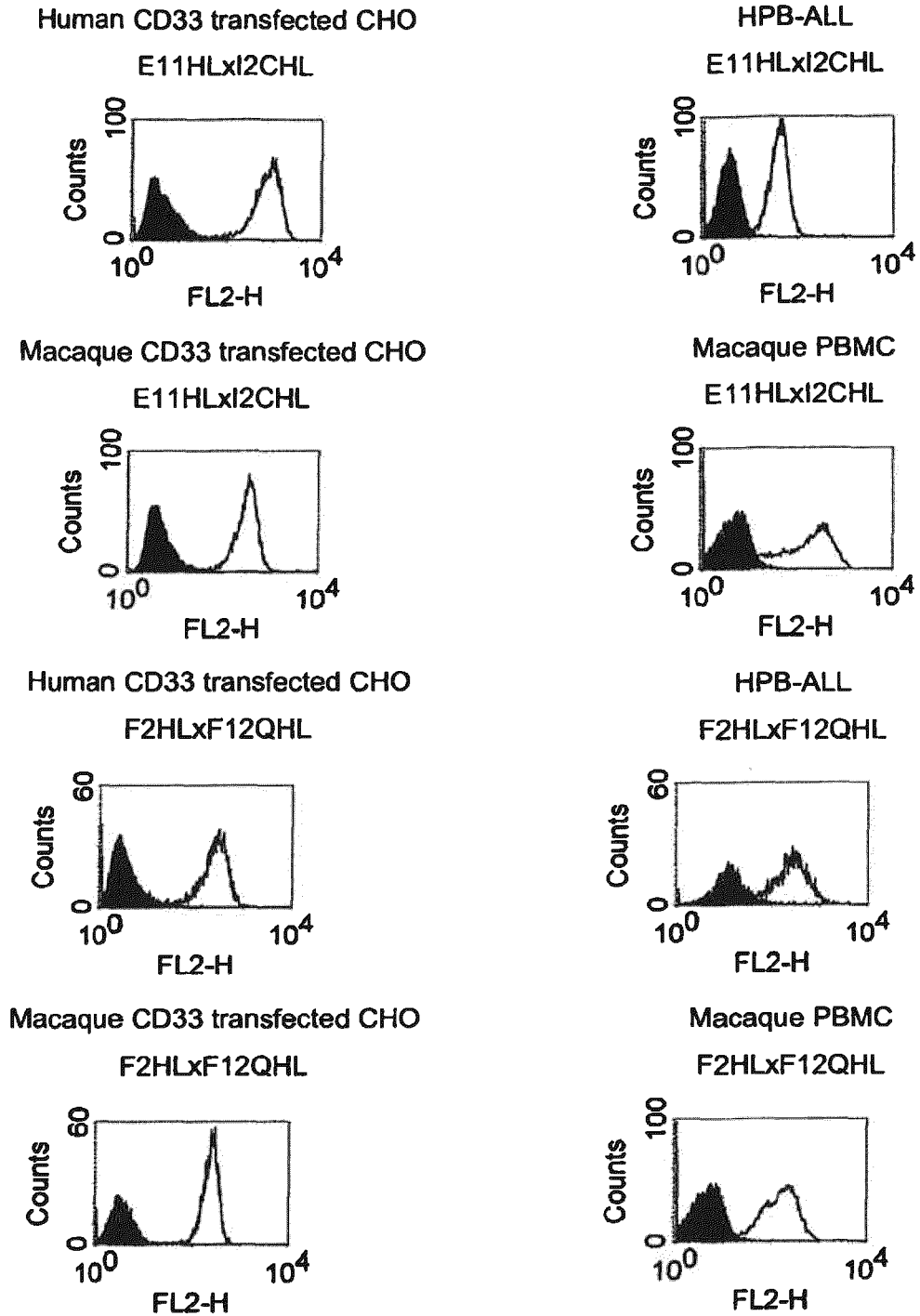


Figure 29(11)

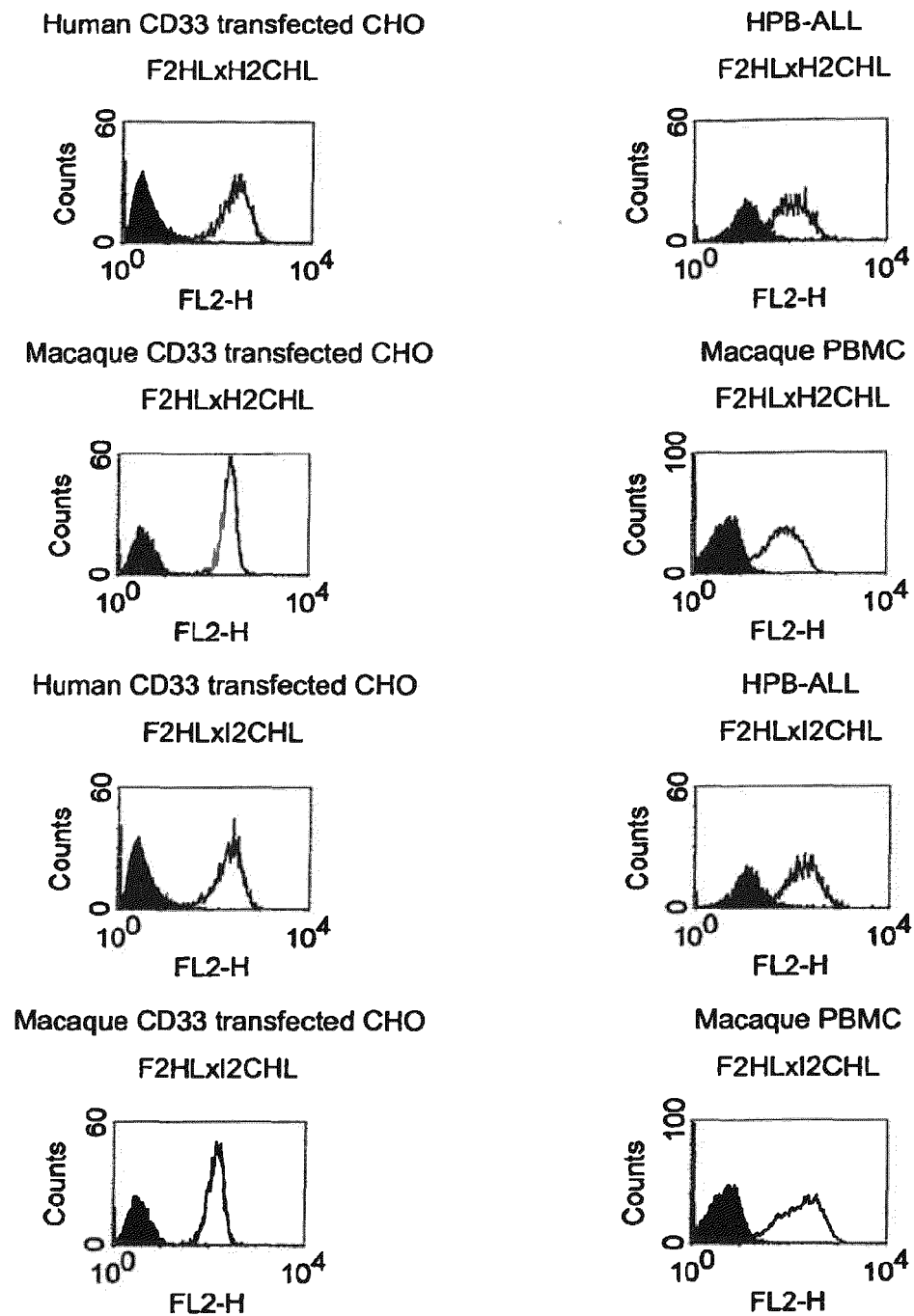
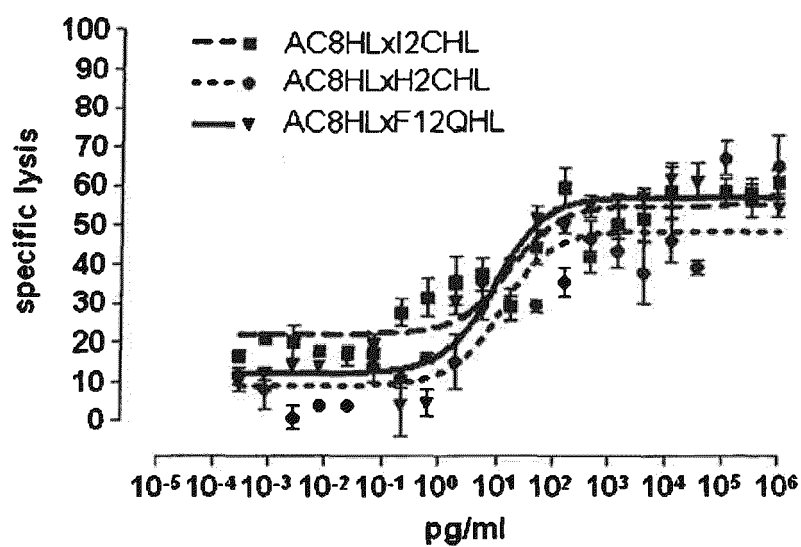


Figure 29(12)

Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human CD33



Effector cells: macaque 4119 LnPx

Target cells: CHO transfected with macaque CD33

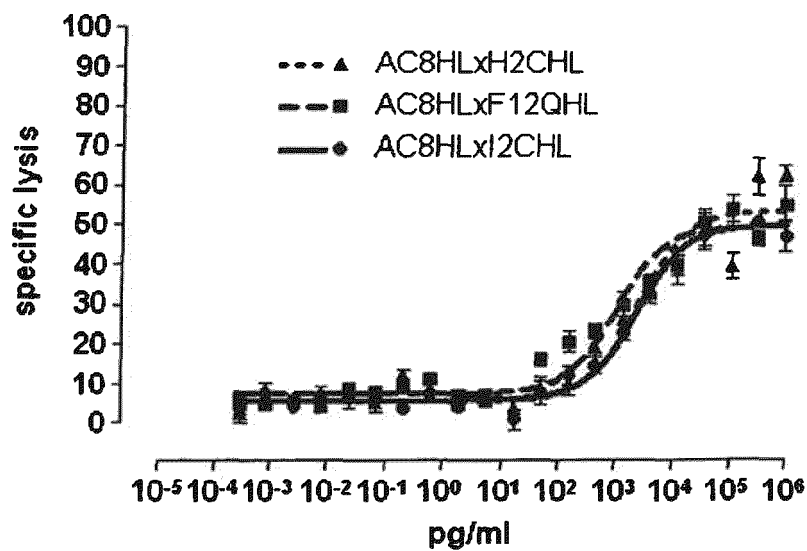
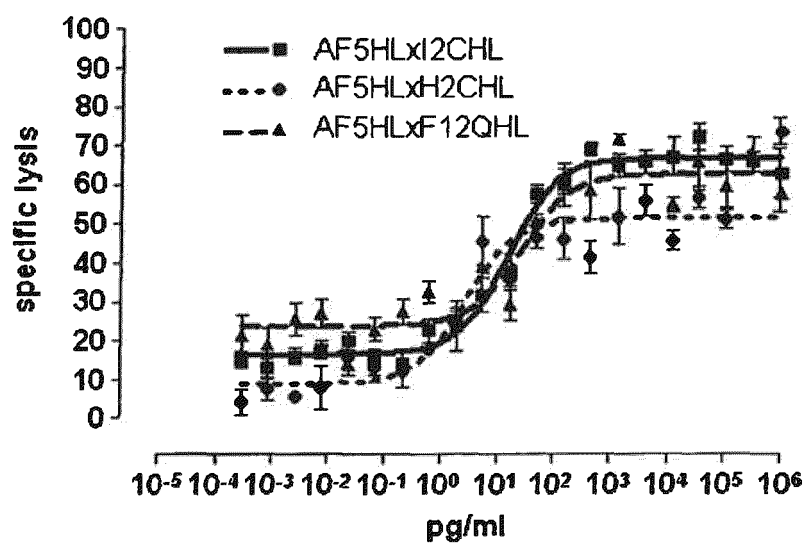


Figure 30(1)

Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human CD33



Effector cells: macaque 4119 LnPx

Target cells: CHO transfected with macaque CD33

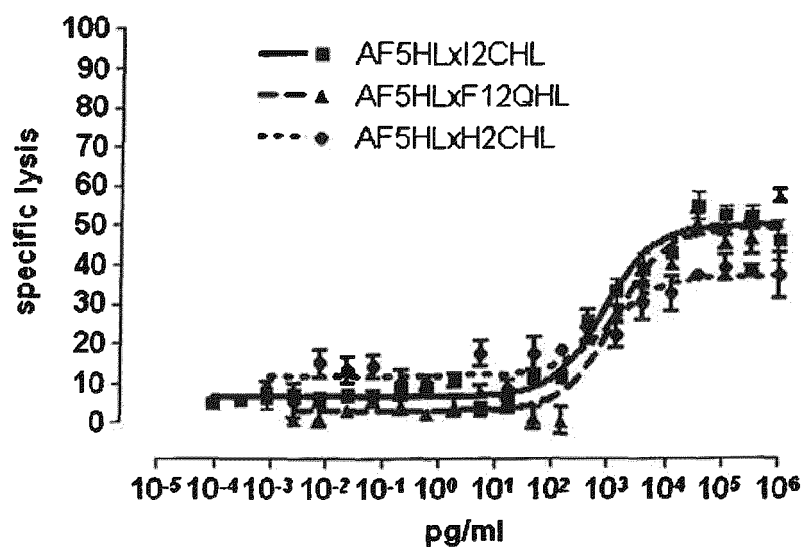
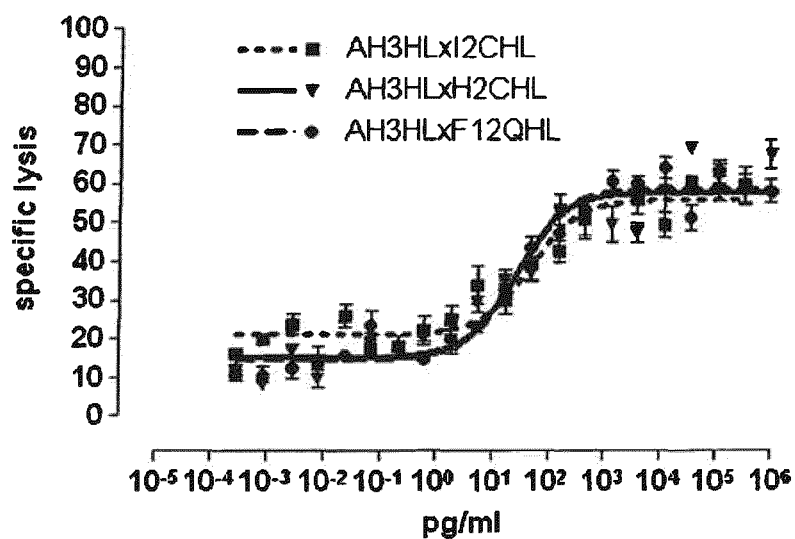


Figure 30(2)

Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human CD33



Effector cells: macaque 4119 LnPx

Target cells: CHO transfected with macaque CD33

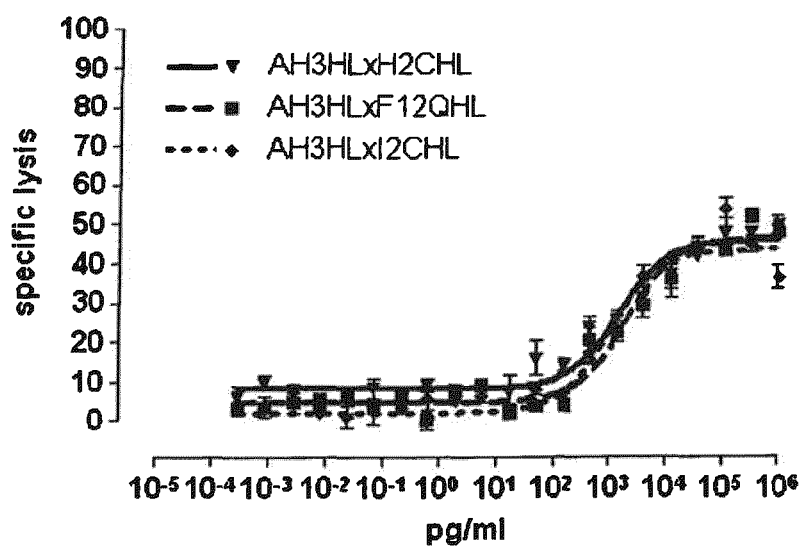
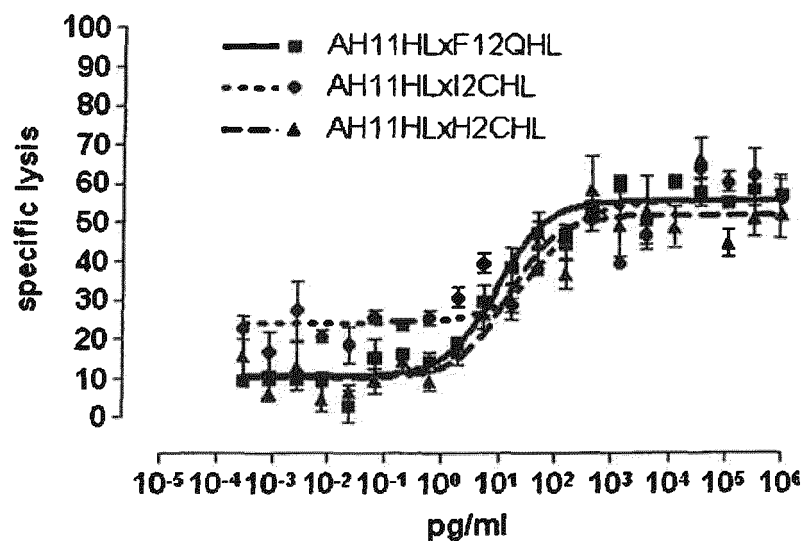


Figure 30(3)

Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human CD33



Effector cells: macaque 4119 LnPx

Target cells: CHO transfected with macaque CD33

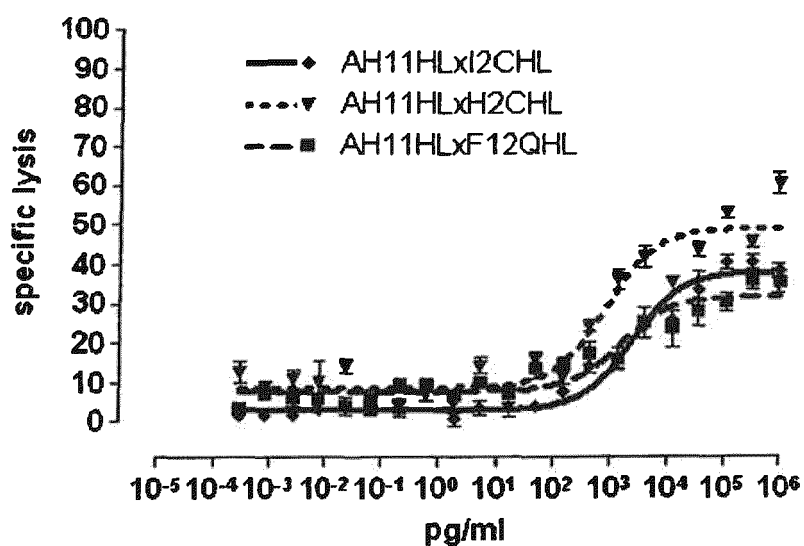
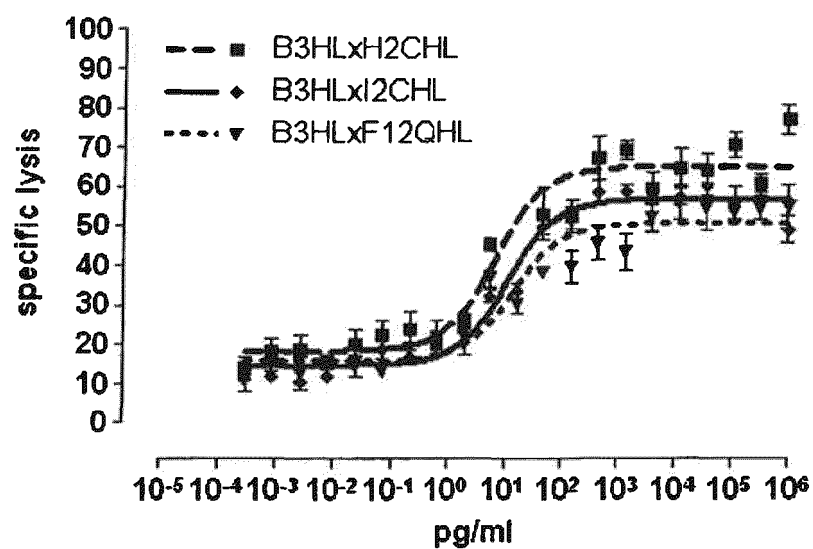


Figure 30(4)

Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human CD33



Effector cells: macaque 4119 LnPx

Target cells: CHO transfected with macaque CD33

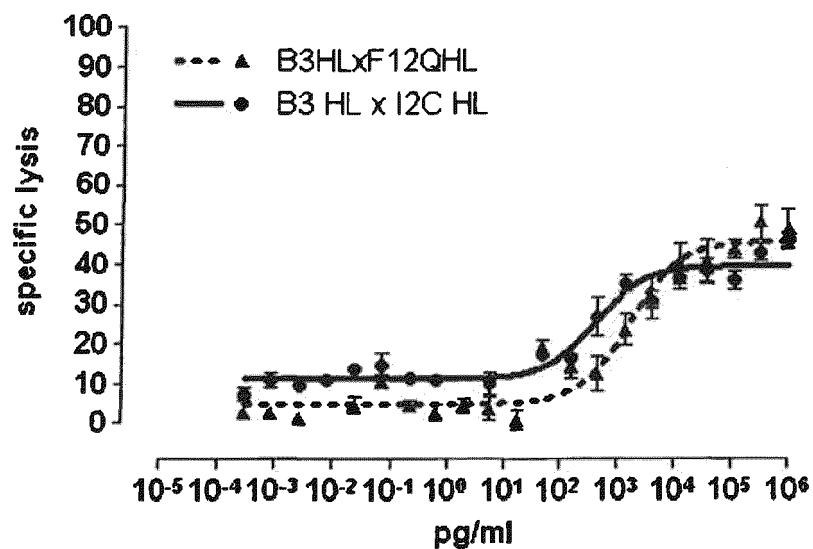
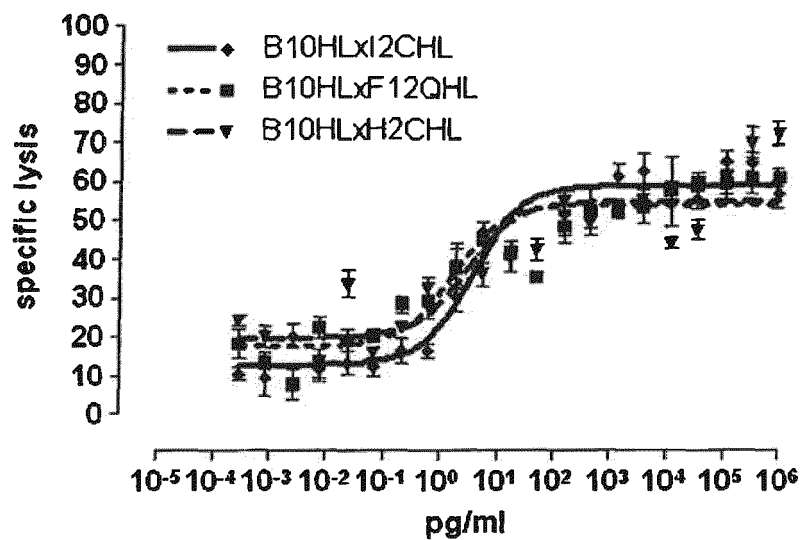


Figure 30(5)

Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human CD33



Effector cells: macaque 4119 LnPx

Target cells: CHO transfected with macaque CD33

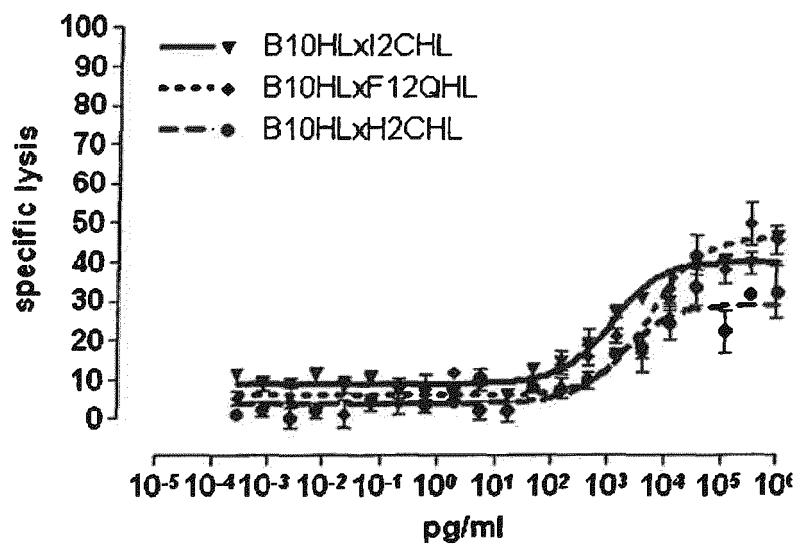
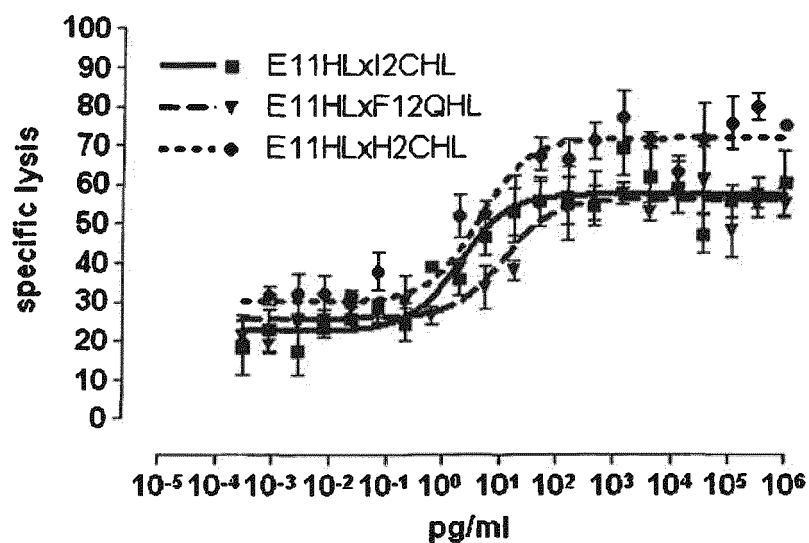


Figure 30(6)

Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human CD33



Effector cells: macaque 4119 LnPx

Target cells: CHO transfected with macaque CD33

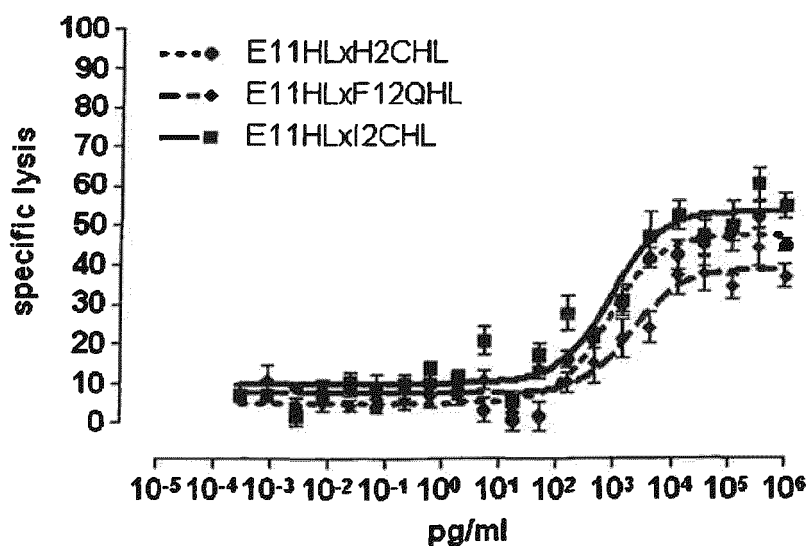
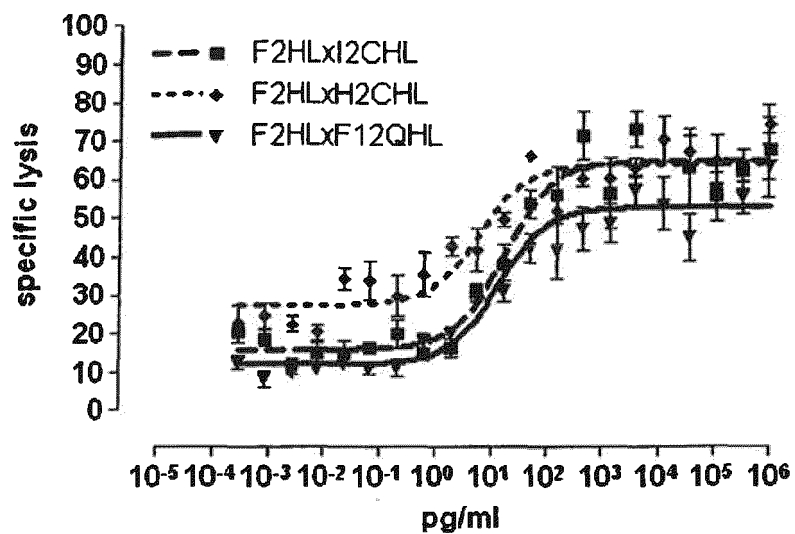


Figure 30(7)

Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human CD33



Effector cells: macaque 4119 LnPx

Target cells: CHO transfected with macaque CD33

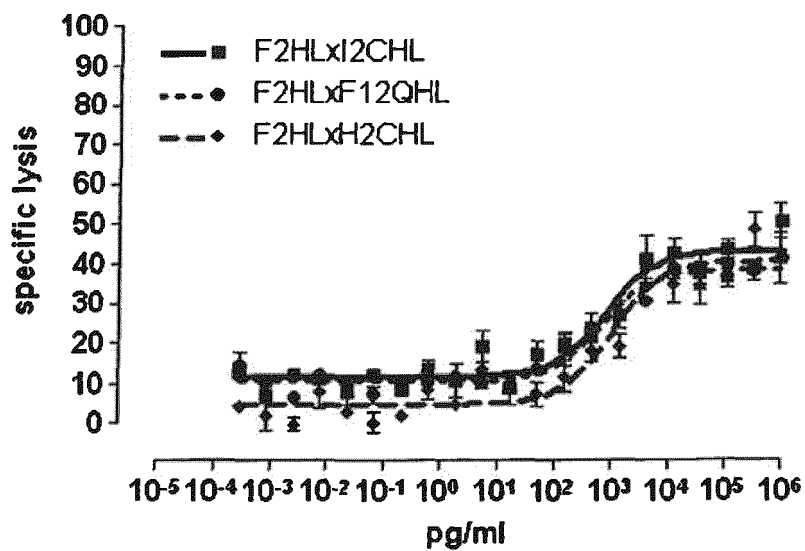


Figure 30(8)

Figure 31

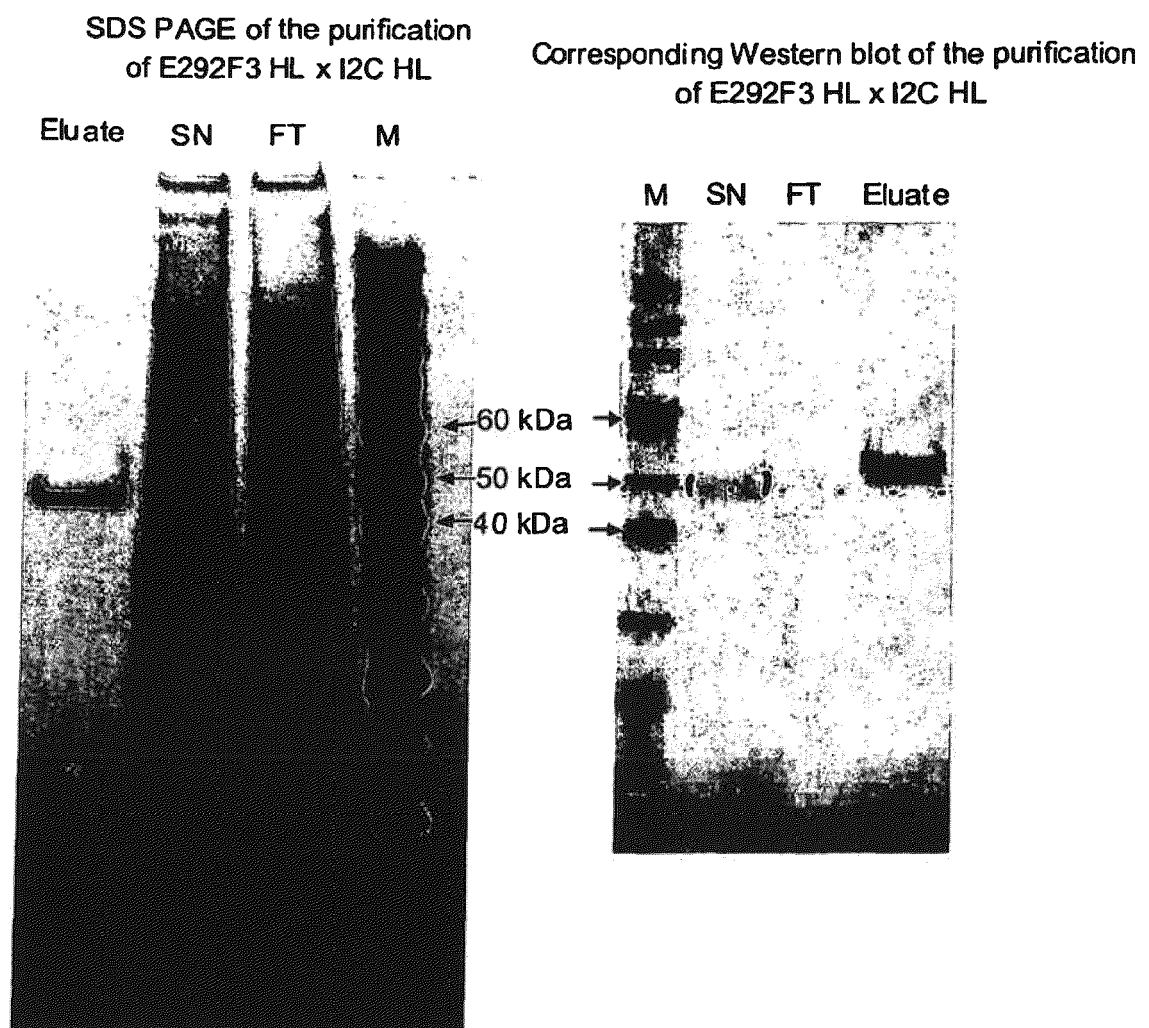


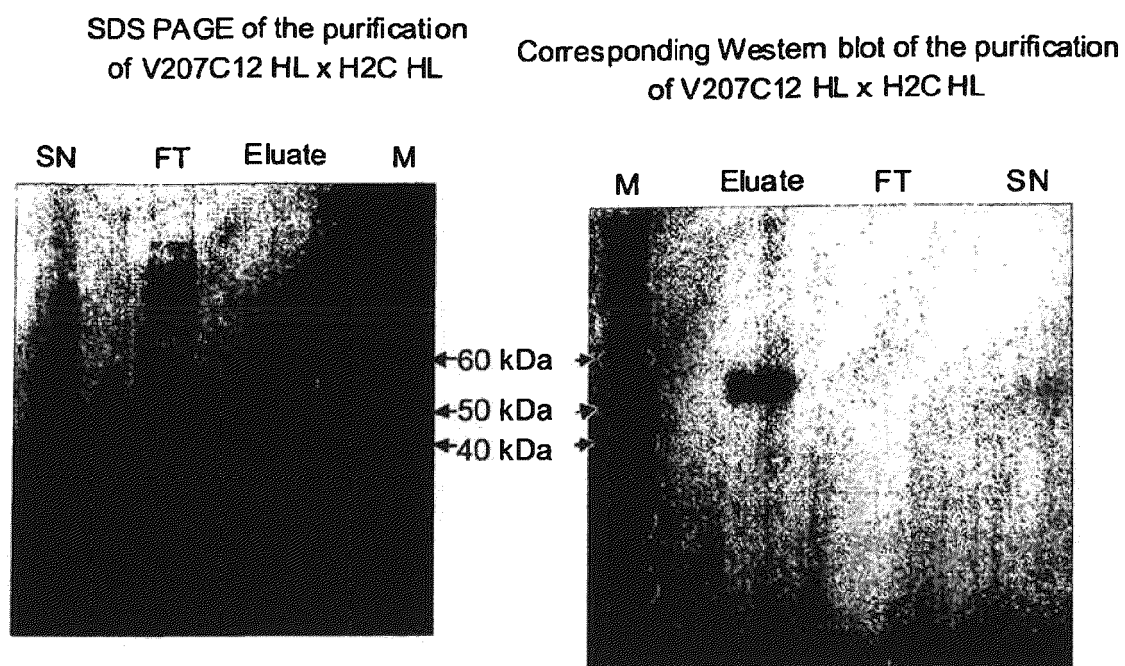
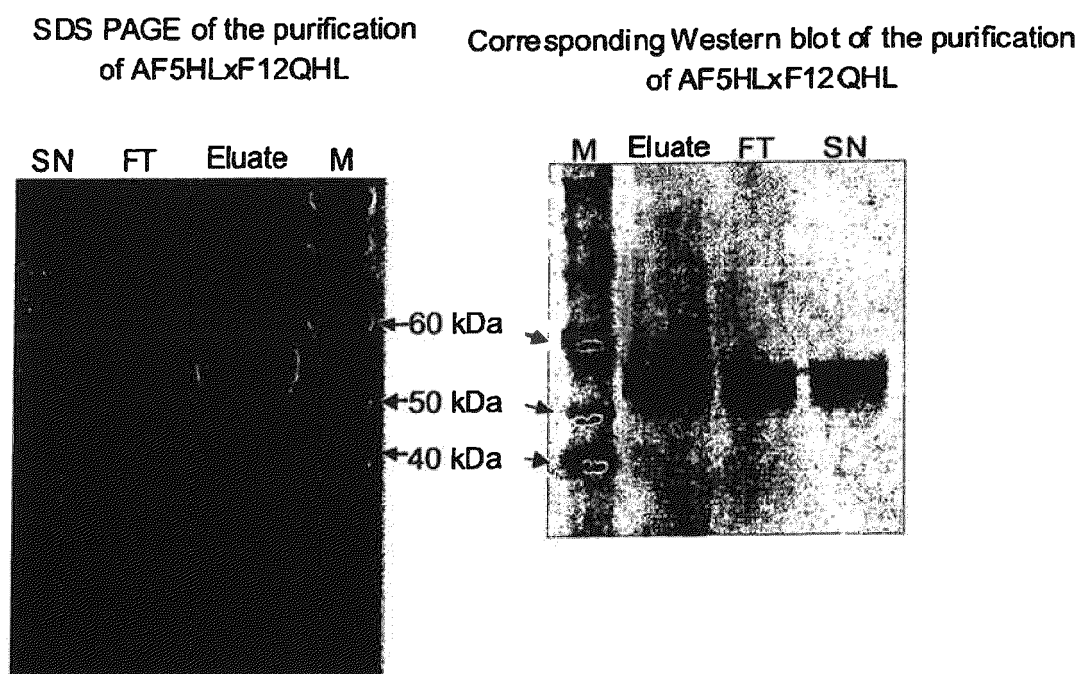
Figure 32**Figure 33**

Figure 34

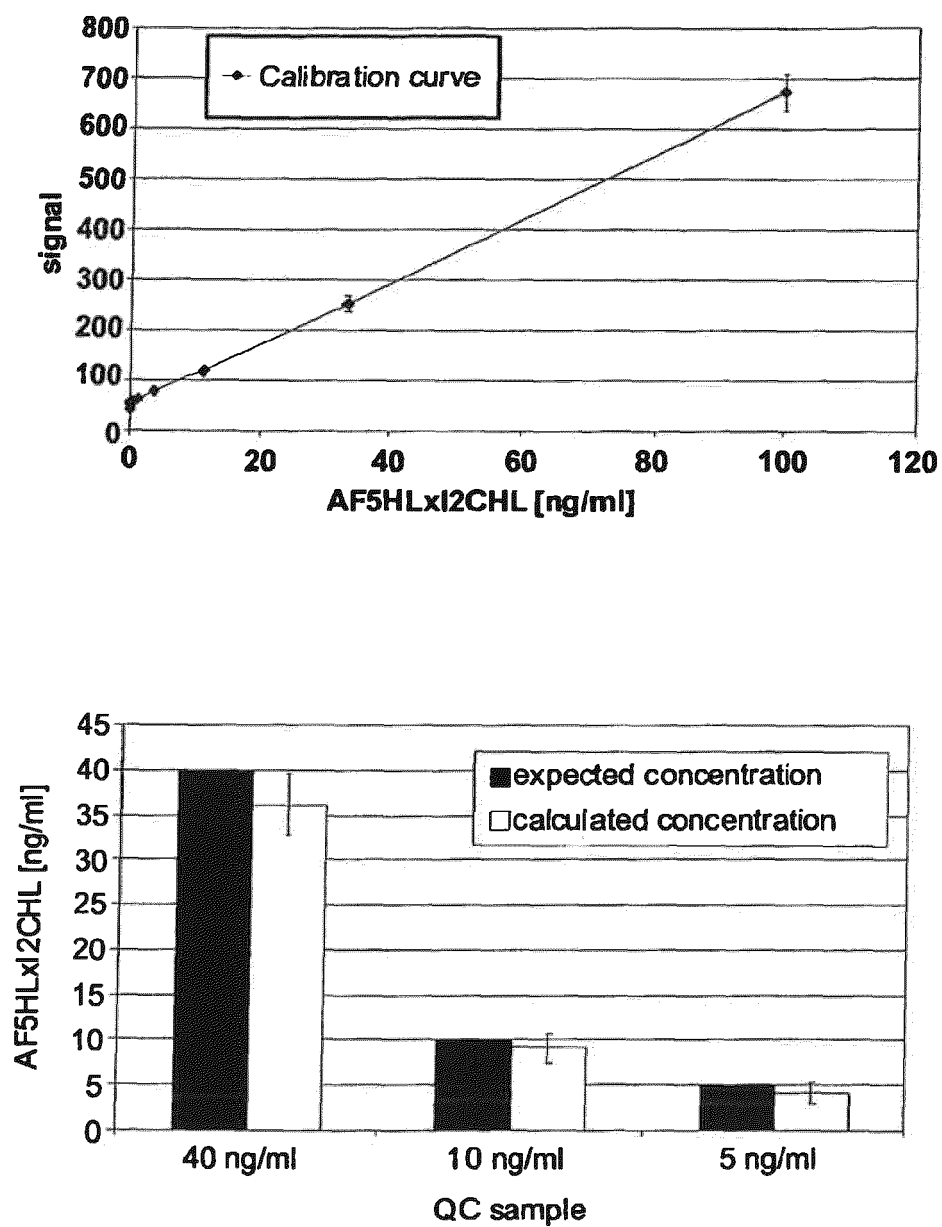


Figure 35

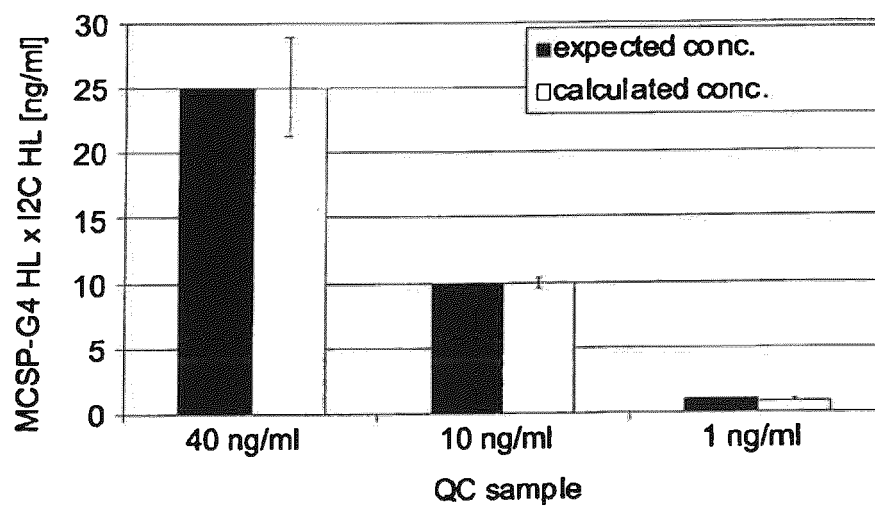
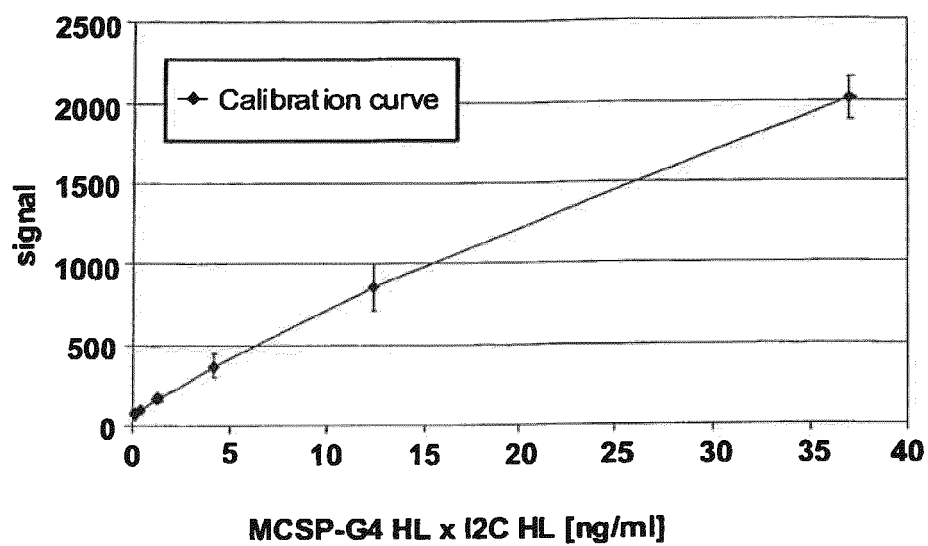


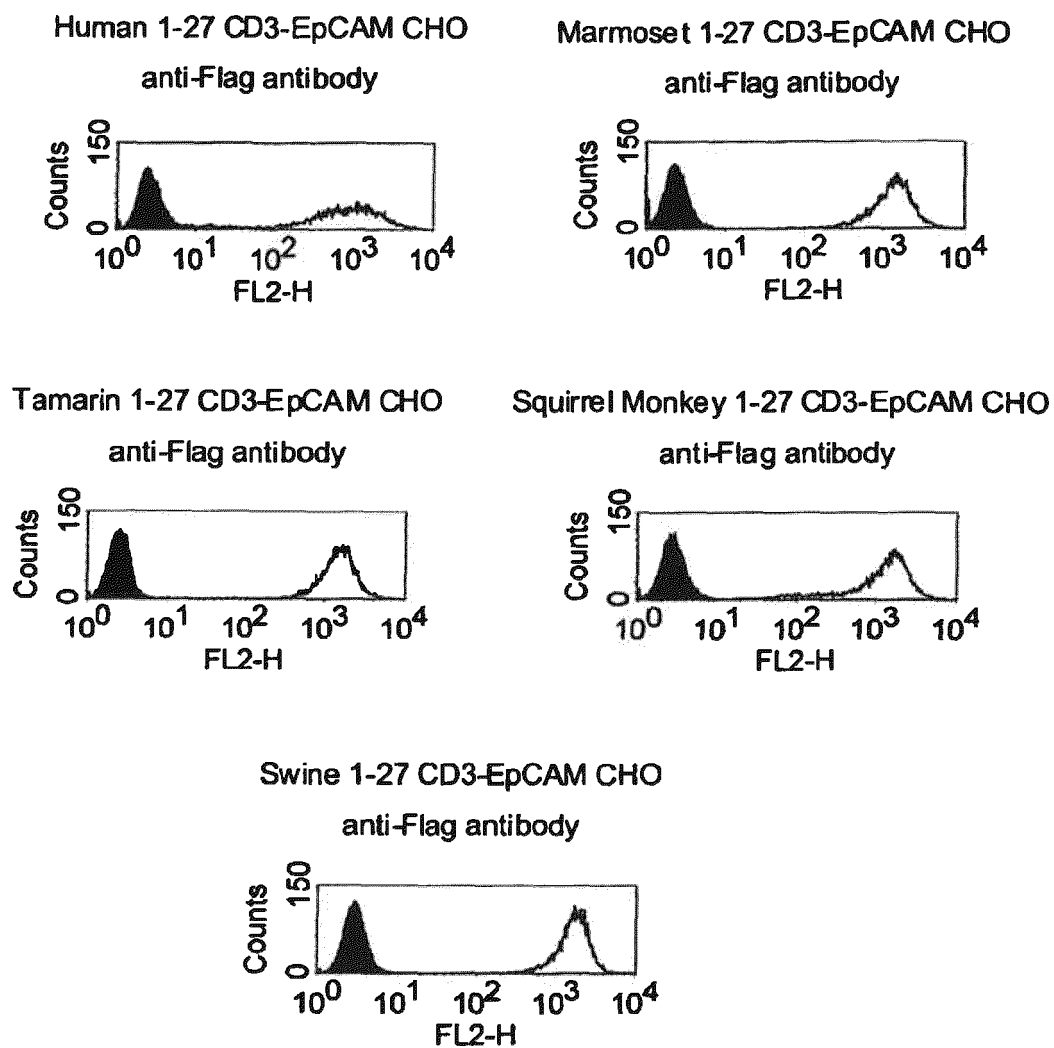
Figure 36

Figure 37

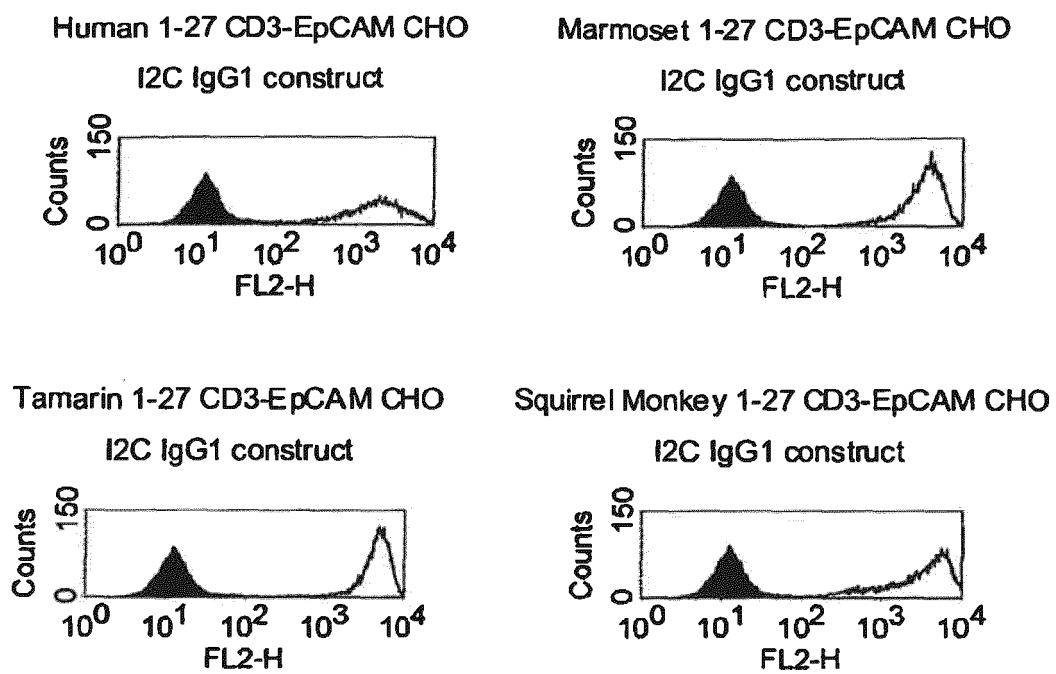
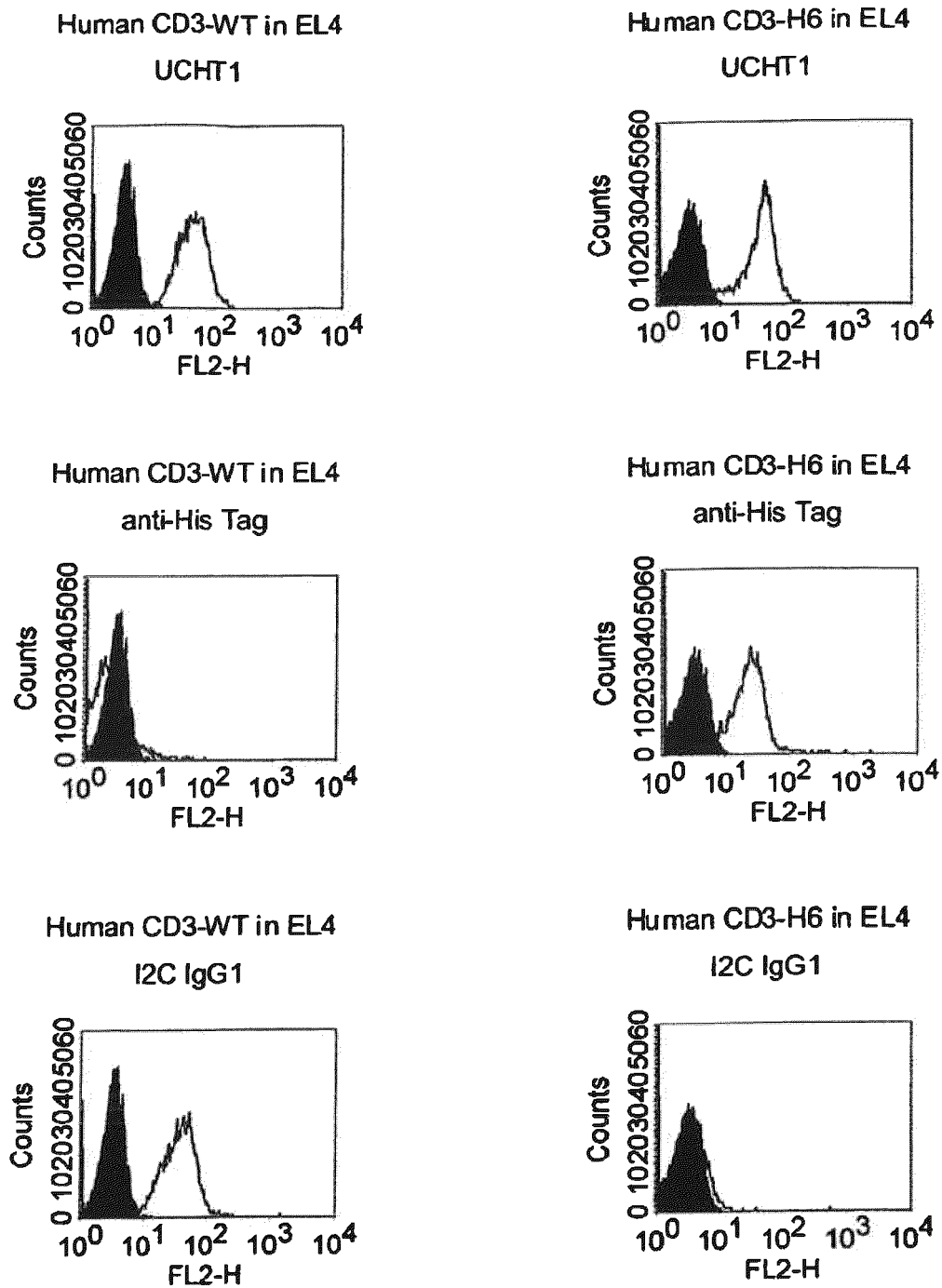


Figure 38

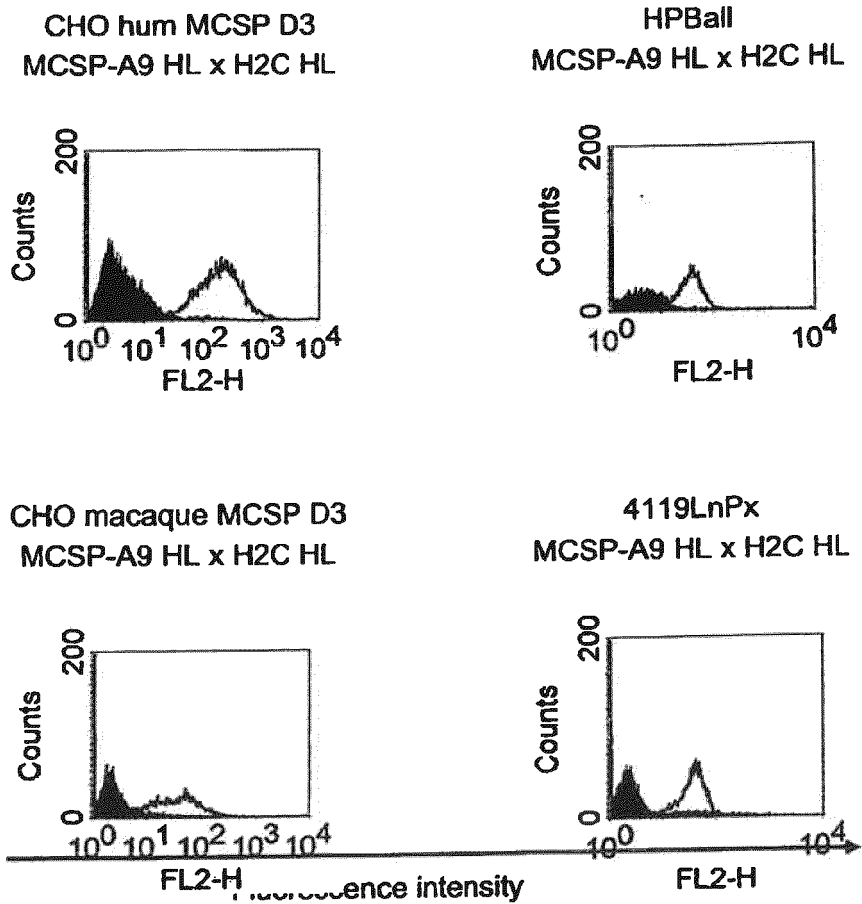
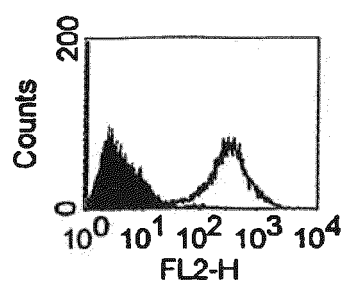
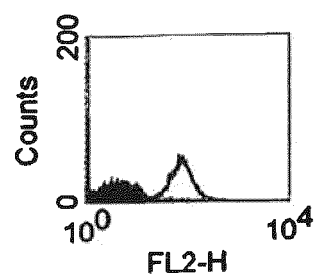


Figure 39a

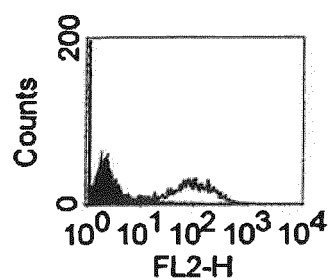
CHO hum MCSP D3
MCSP-A9 HL x F12Q HL



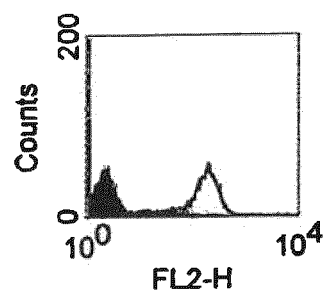
HPBall
MCSP-A9 HL x F12Q HL



CHO macaque MCSP D3
MCSP-A9 HL x F12Q HL



4119LnPx
MCSP-A9 HL x F12Q HL



Fluorescence intensity

Figure 39b

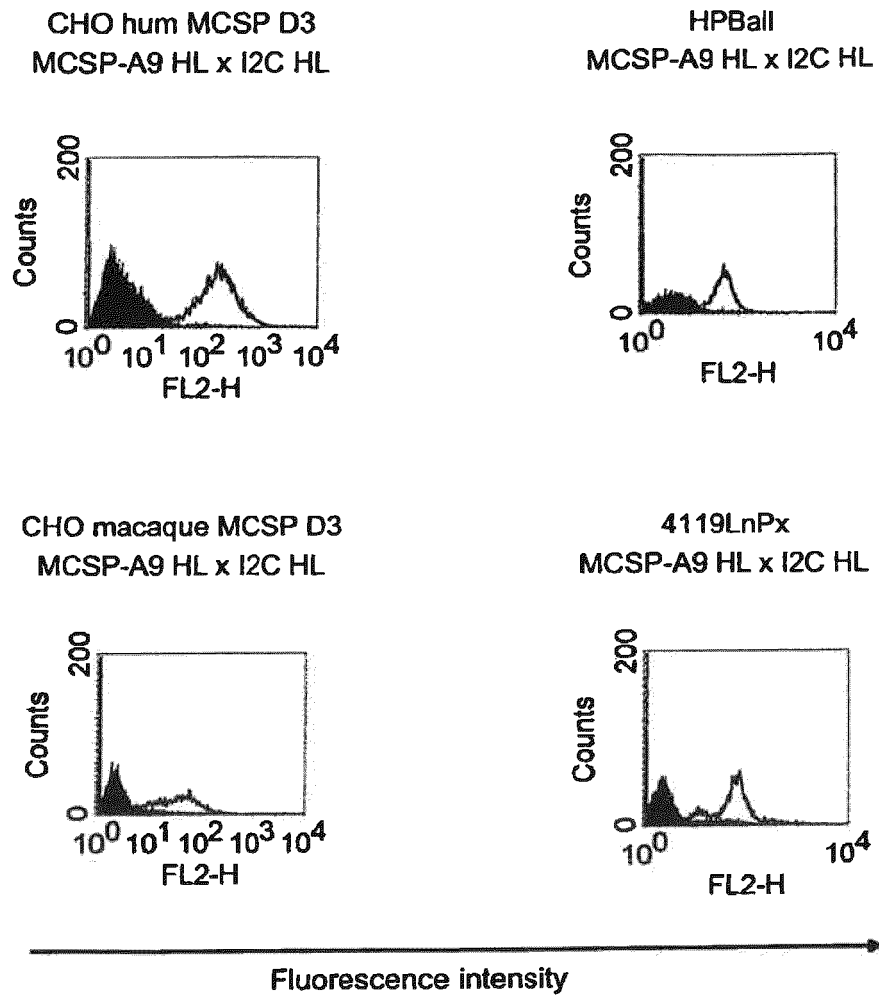


Figure 39c

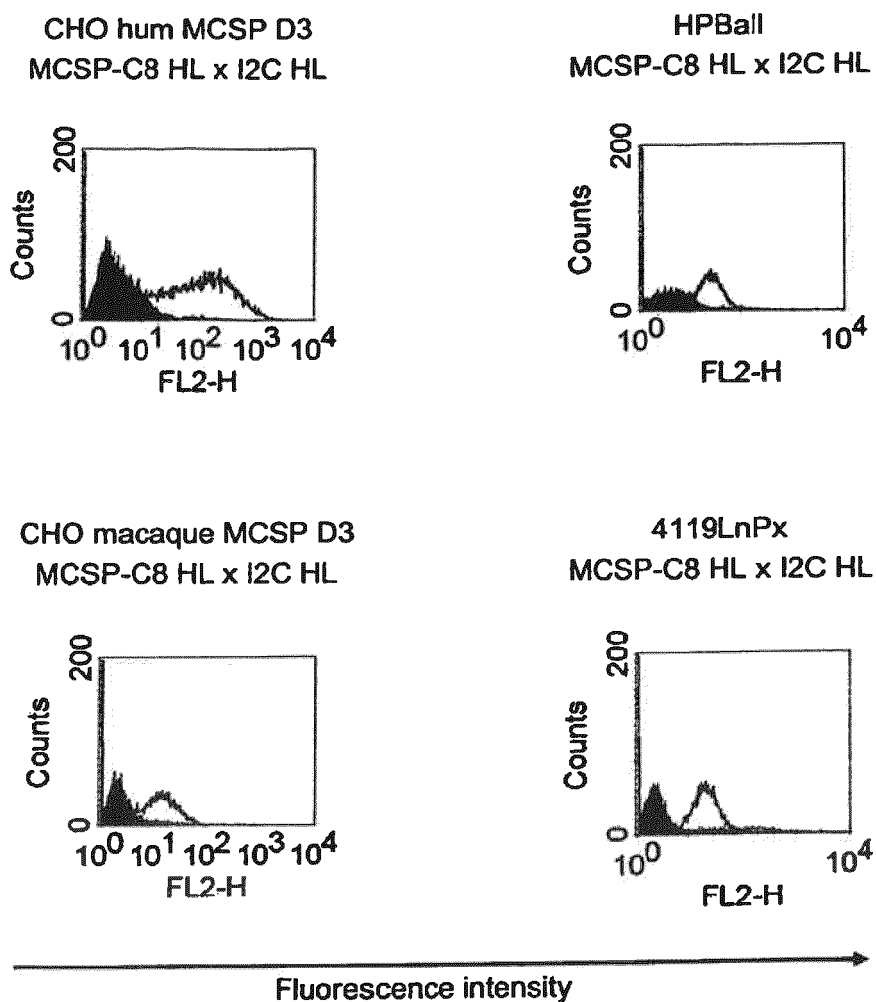


Figure 39d

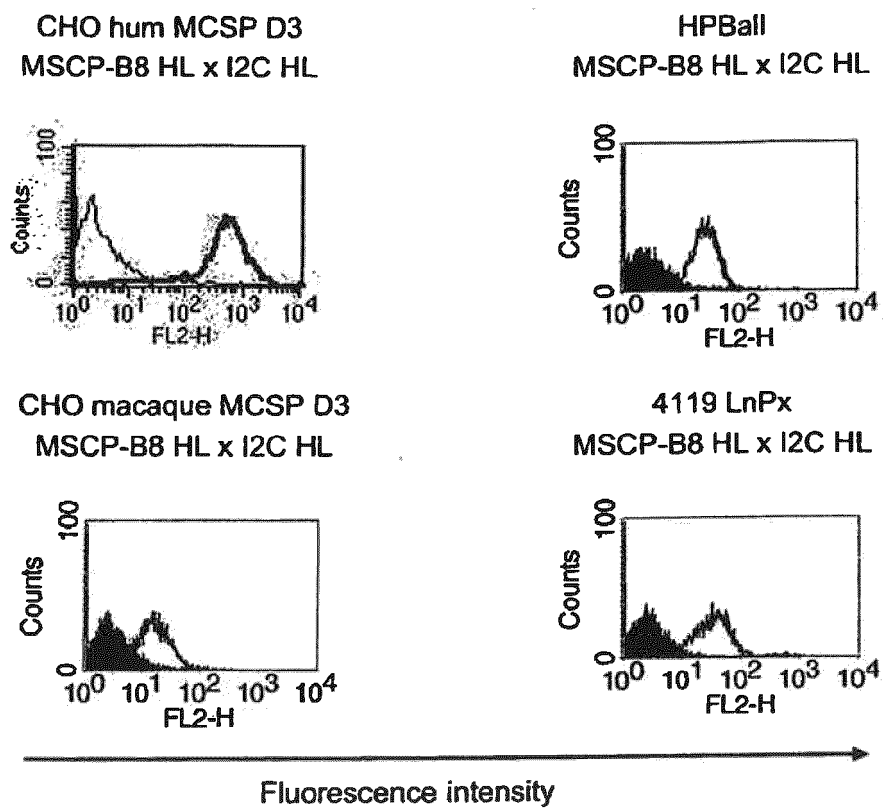


Figure 39e

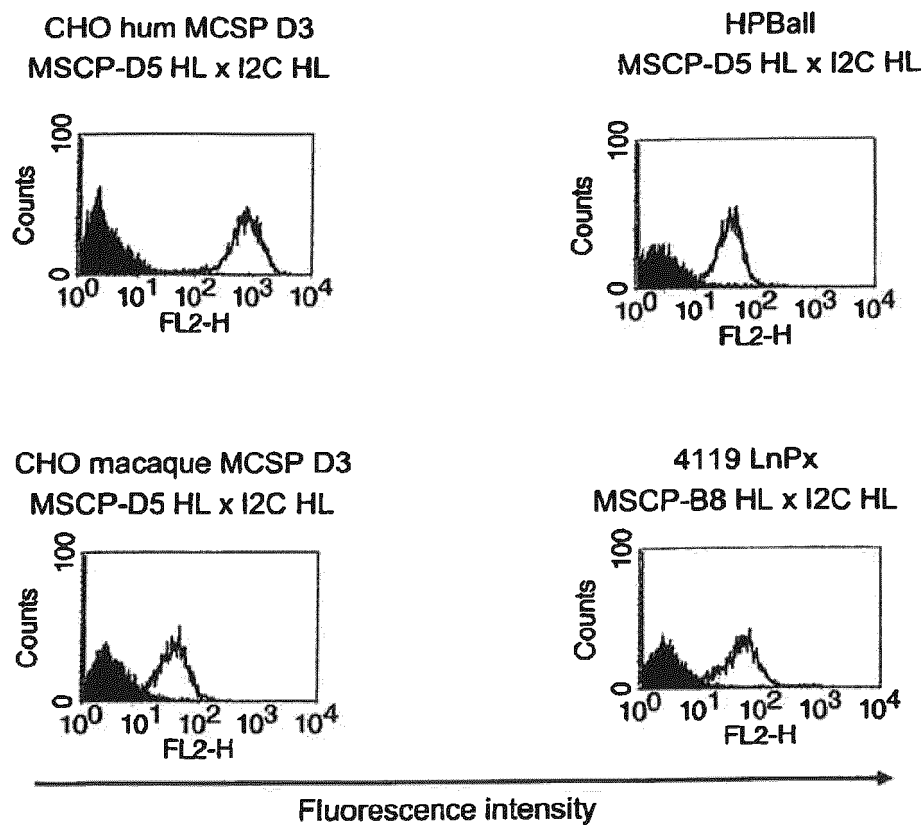


Figure 39f

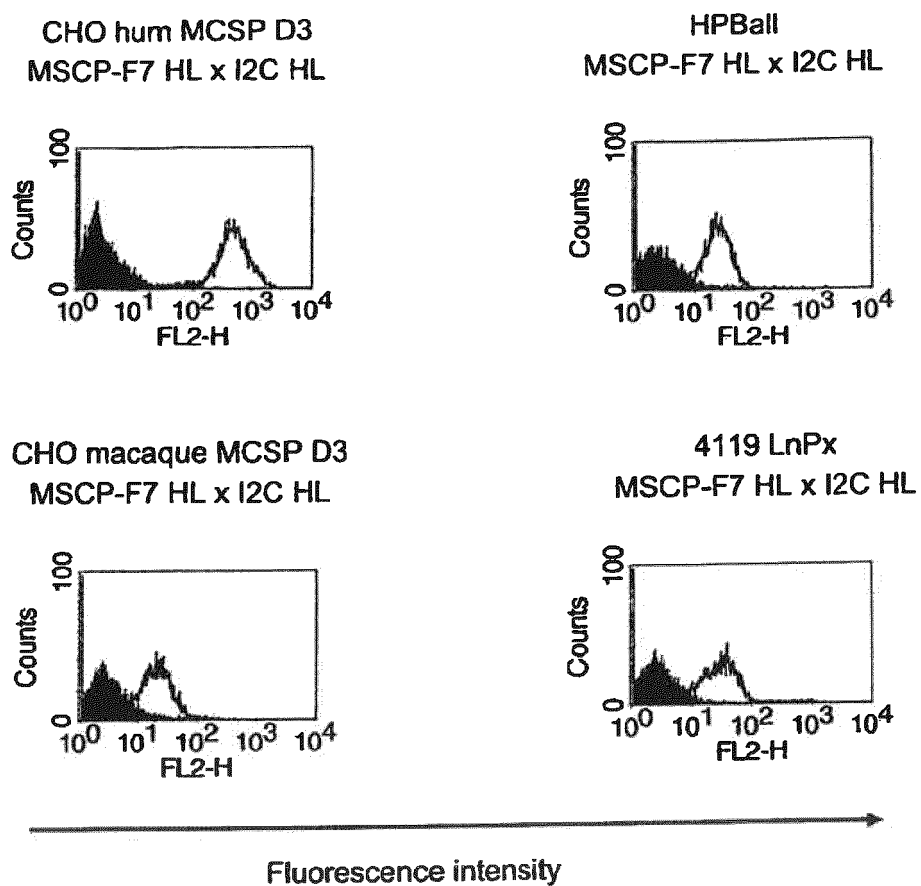


Figure 39g

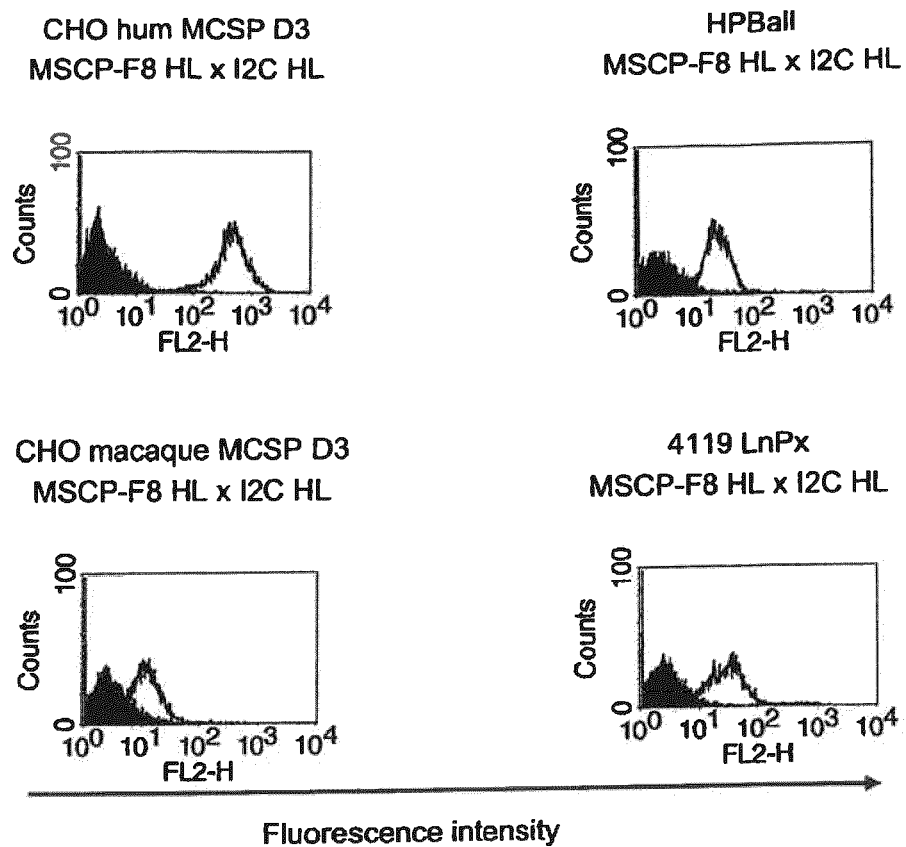


Figure 39h

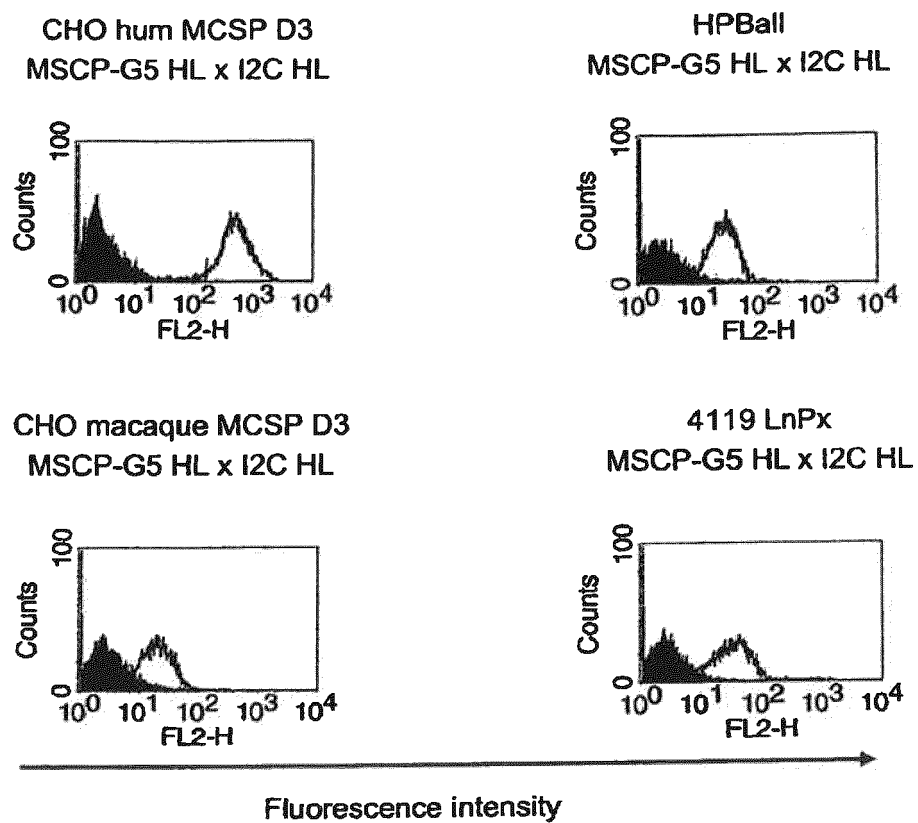
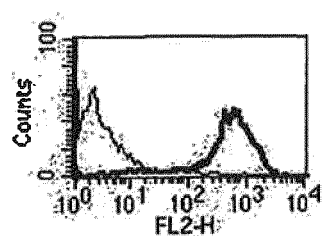
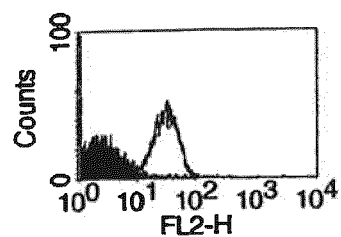


Figure 39i

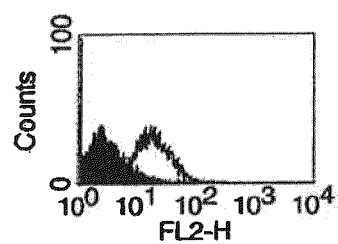
CHO hum MCSP D3
MSCP-G8 HL x I2C HL



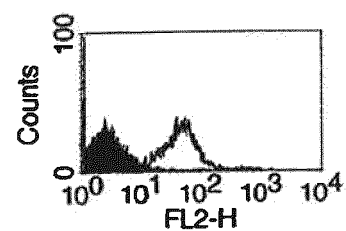
HPBall
MSCP-G8 HL x I2C HL



CHO macaque MCSP D3
MSCP-G8 HL x I2C HL



4119 LnPx
MSCP-G8 HL x I2C HL



Fluorescence intensity

Figure 39j

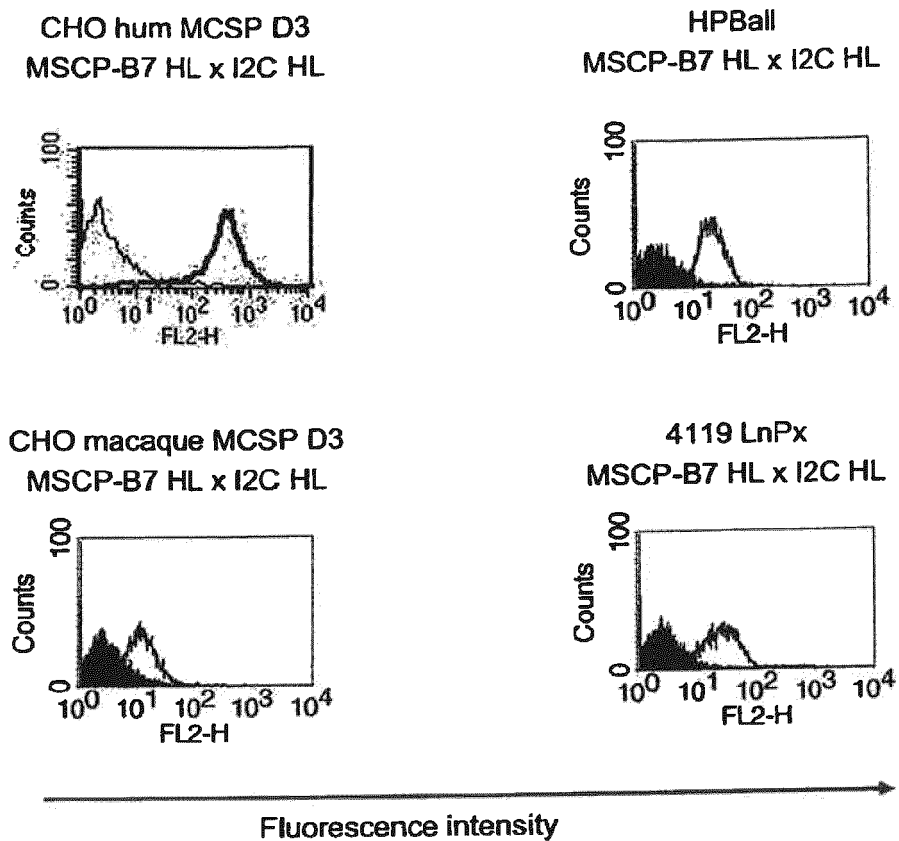


Figure 39k

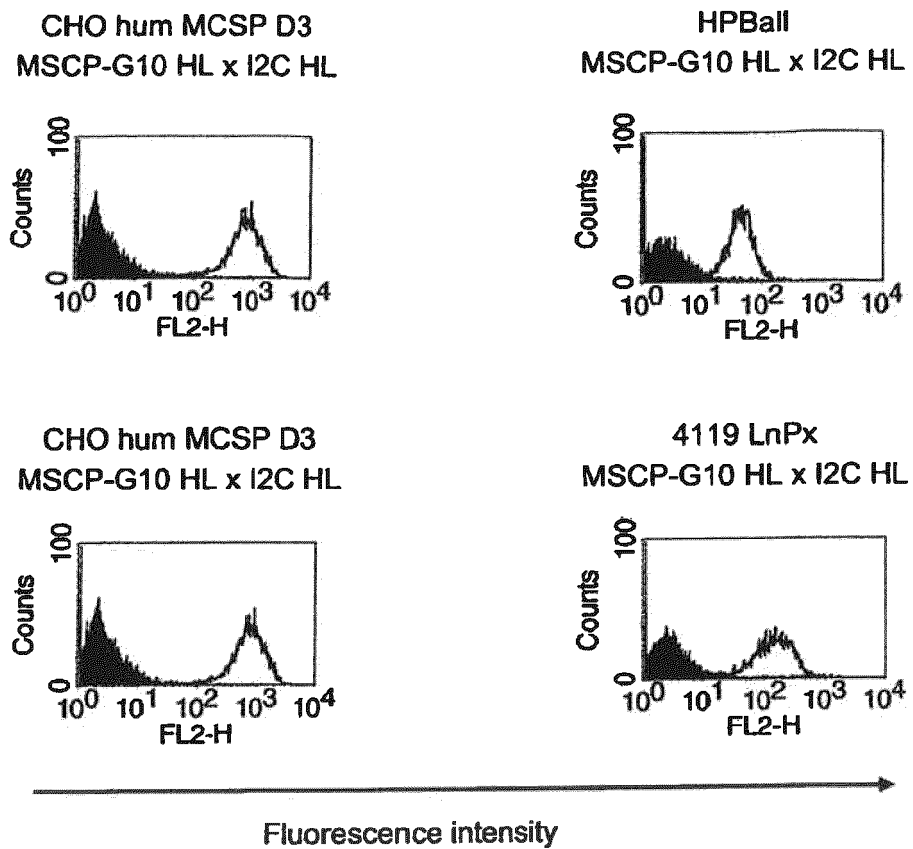
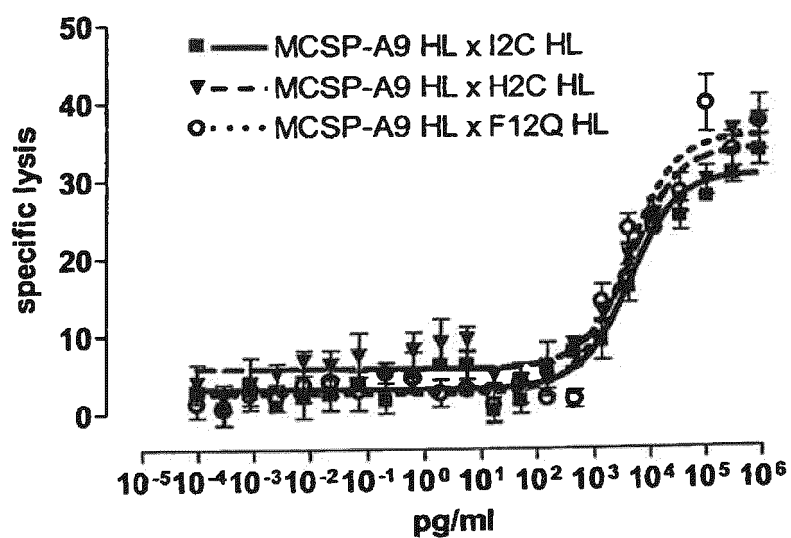


Figure 39I

Figure 40a

Effector cells: stimulated human CD4/CD56 depleted human PBMC
 Target cells: CHO transfected with human MCSP D3
 E:T ratio: 10:1



Effector cells: 4119 LnPx
 Target cells: CHO transfected with macaque MCSP D3
 E:T ratio: 10:1

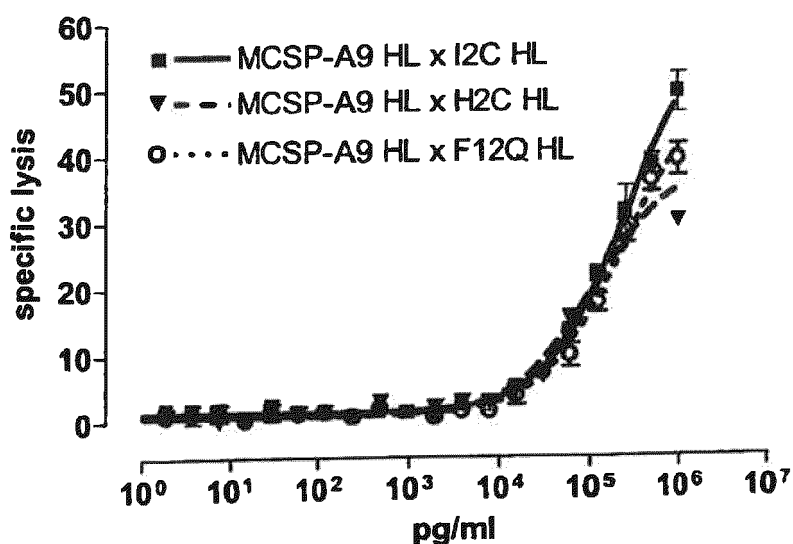
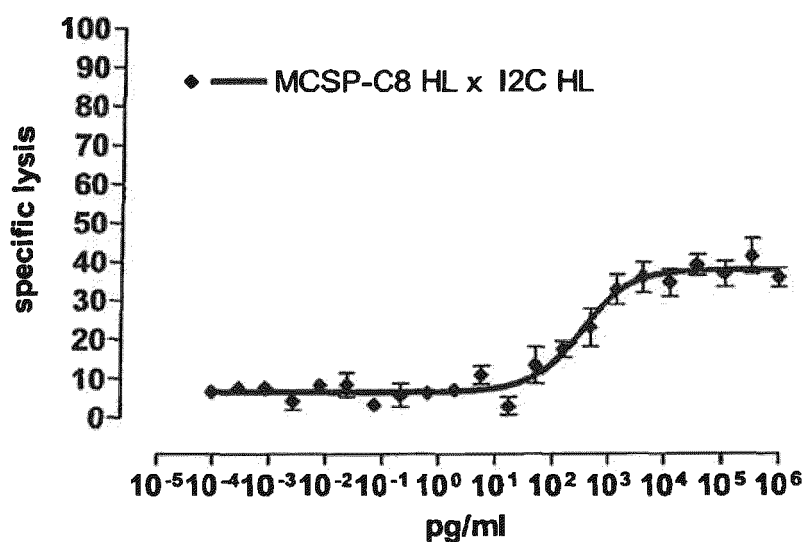


Figure 40b

Effector cells: stimulated human CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human MCSP D3

E:T ratio: 10:1



Effector cells: 4119 LnPx

Target cells: CHO transfected with macaque MCSP D3

E:T ratio: 10:1

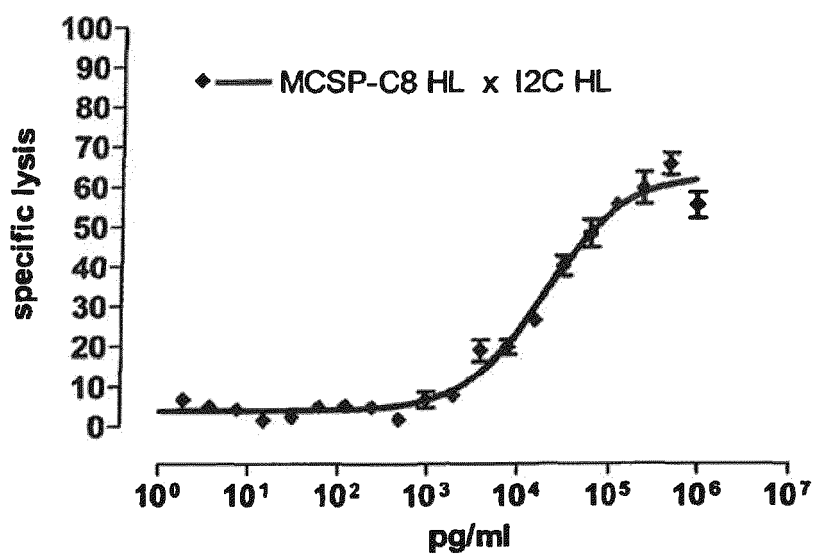
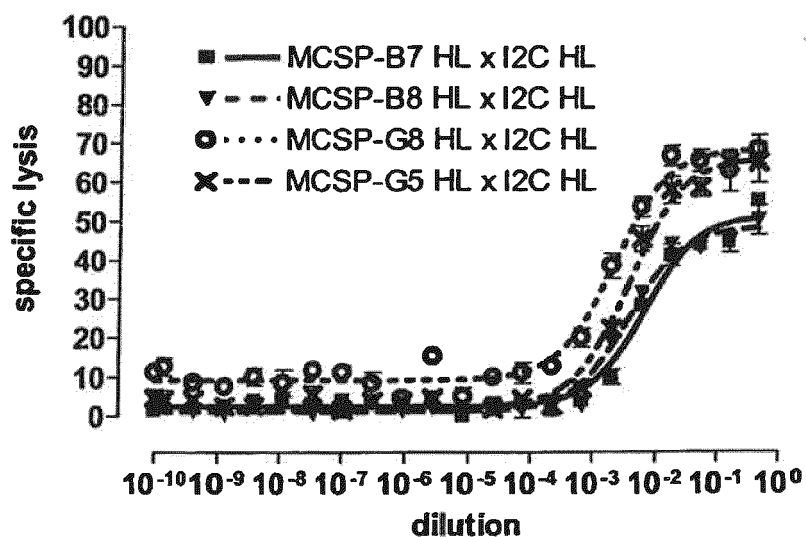


Figure 40c

Effector cells: stimulated human CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human MCSP D3

E:T ratio: 10:1



Effector cells: 4119 LnPx

Target cells: CHO transfected with macaque MCSP D3

E:T ratio: 10:1

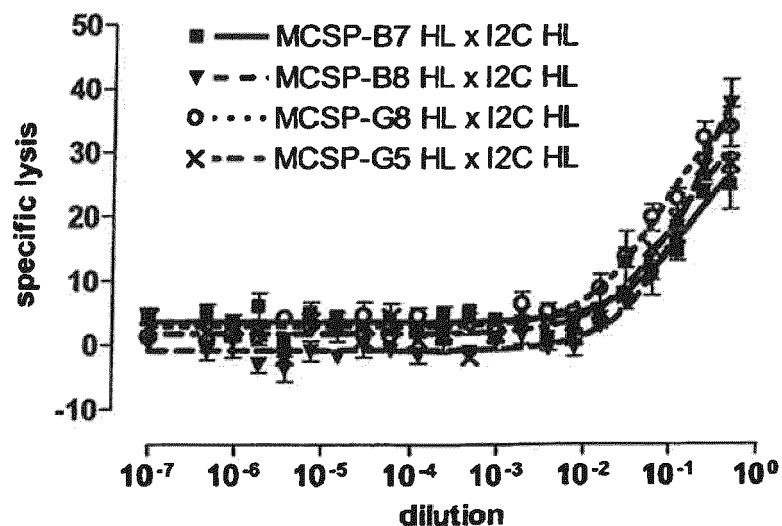
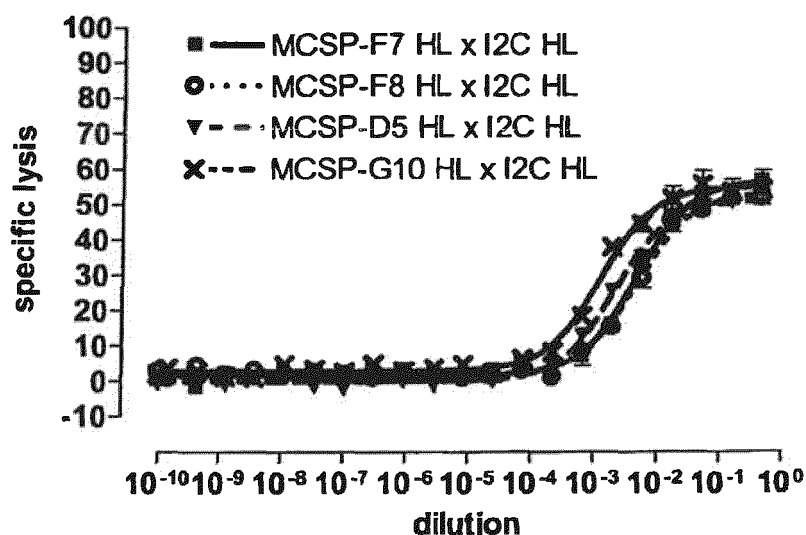


Figure 40d

Effector cells: stimulated human CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human MCSP D3

E:T ratio: 10:1



Effector cells: 4119 LnPx

Target cells: CHO transfected with macaque MCSP D3

E:T ratio: 10:1

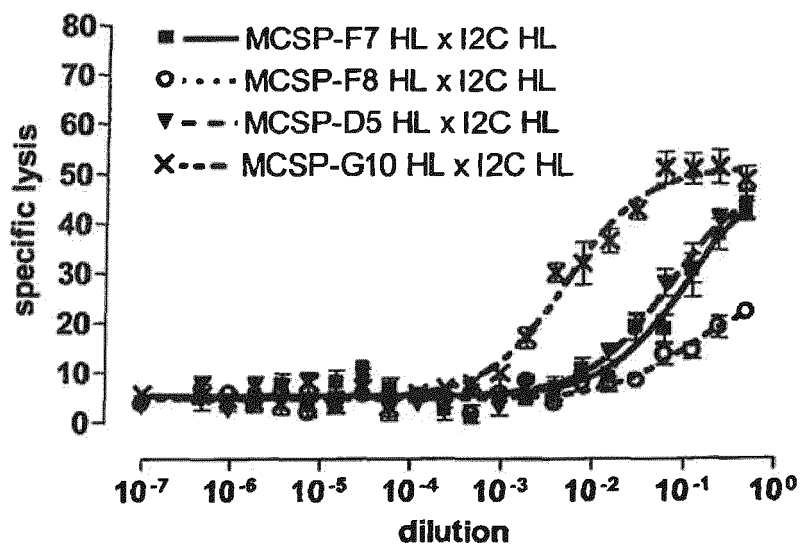
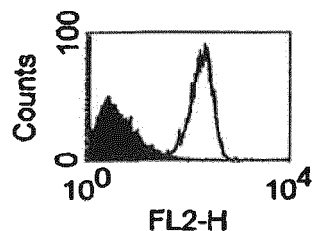


Figure 41a

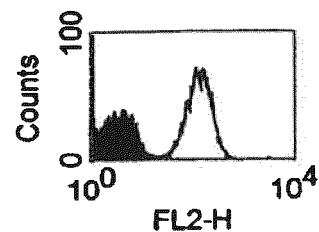
Human CD33 transfected CHO

I2CHLxAF5HL



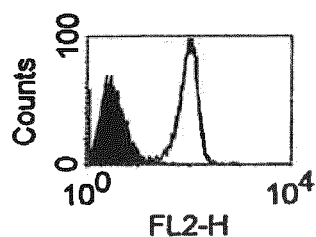
HPB-ALL

I2CHLxAF5HL



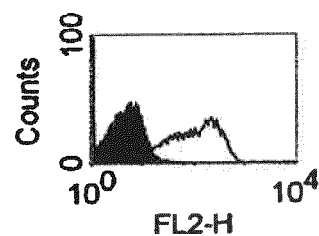
Macaque CD33 transfected CHO

I2CHLxAF5HL



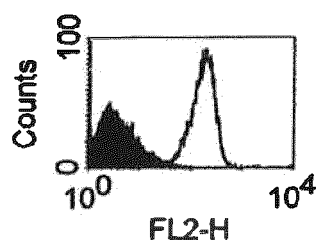
Macaque PBMC

I2CHLxAF5HL



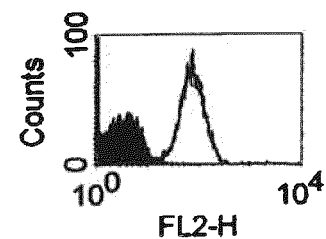
Human CD33 transfected CHO

H2CHLxAF5HL



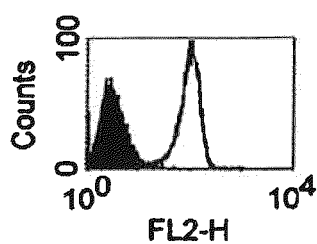
HPB-ALL

H2CHLxAF5HL



Macaque CD33 transfected CHO

H2CHLxAF5HL



Macaque PBMC

H2CHLxAF5HL

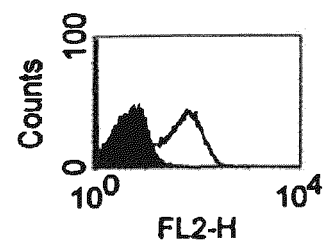
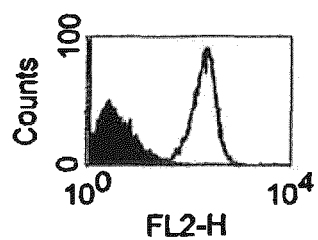


Figure 41b

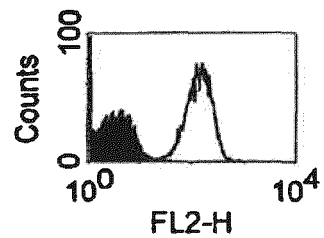
Human CD33 transfected CHO

F12QHLxAF5HL



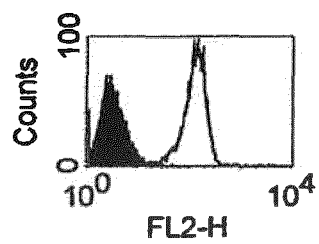
HPB-ALL

F12QHLxAF5HL



Macaque CD33 transfected CHO

F12QHLxAF5HL



Macaque PBMC

F12QHLxAF5HL

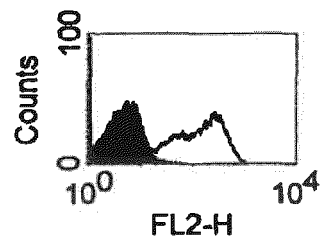
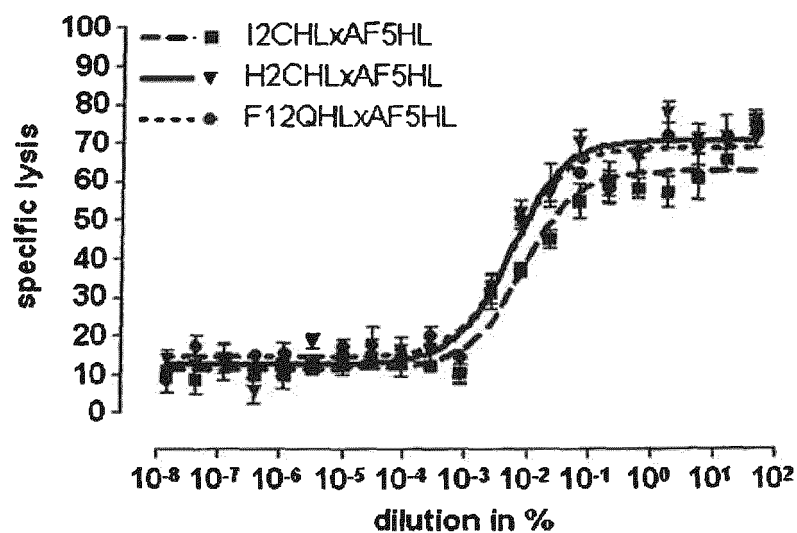


Figure 42

Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: CHO transfected with human CD33



Effector cells: macaque 4119 LnPx

Target cells: CHO transfected with macaque CD33

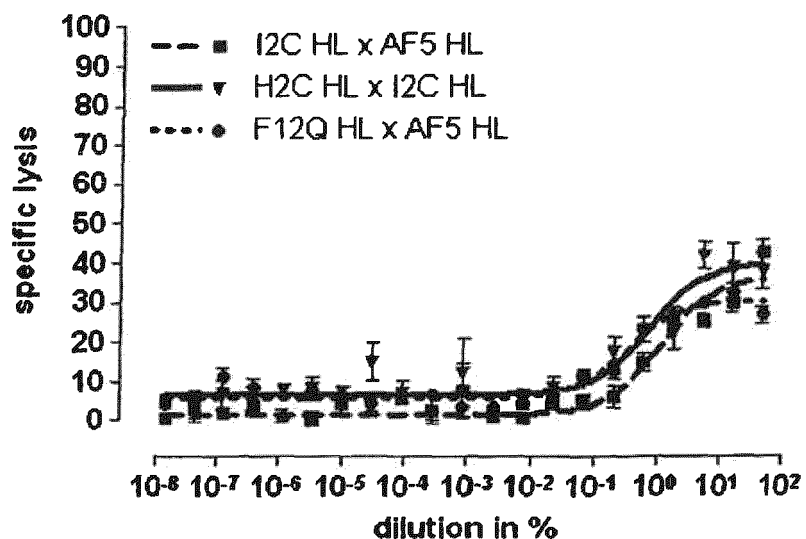


Figure 43

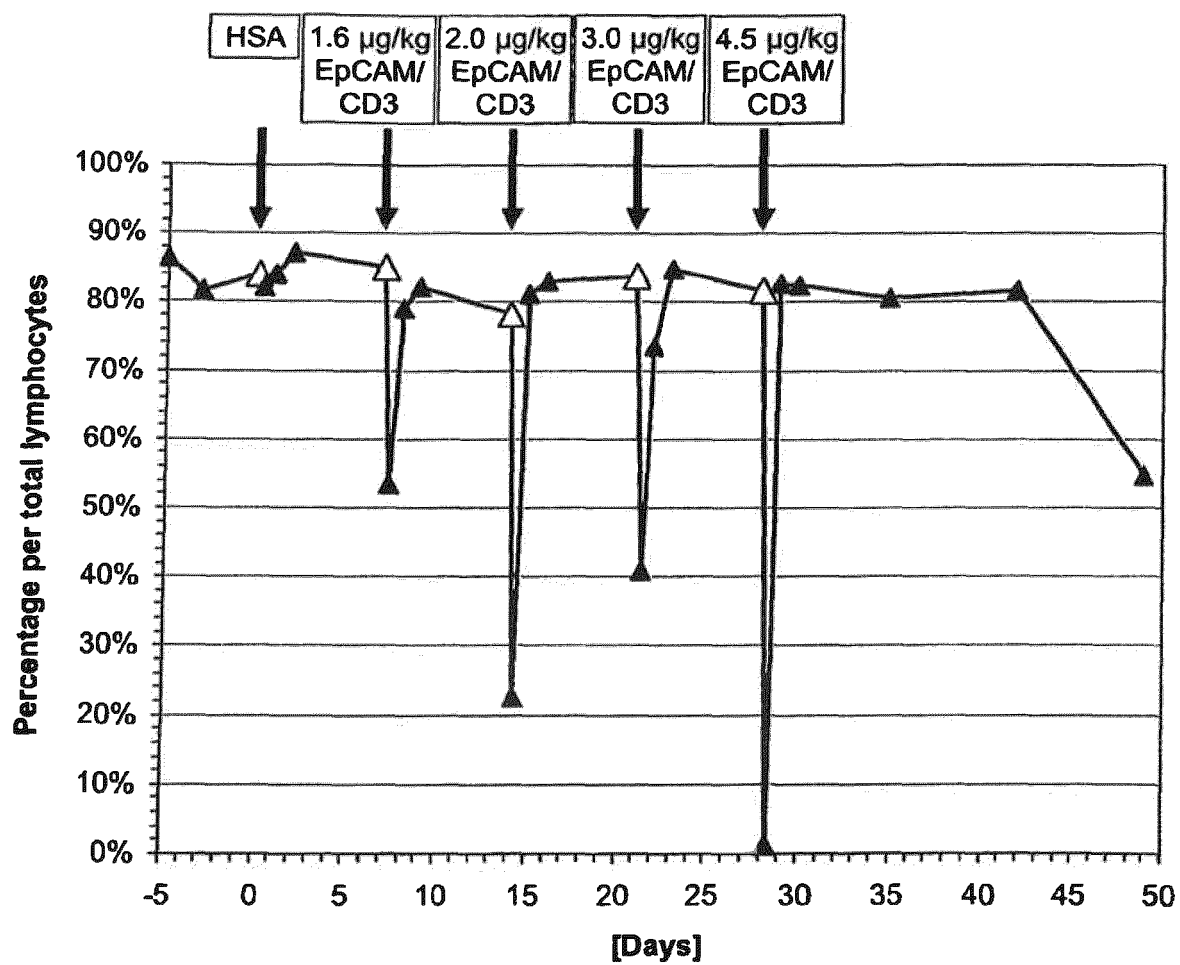


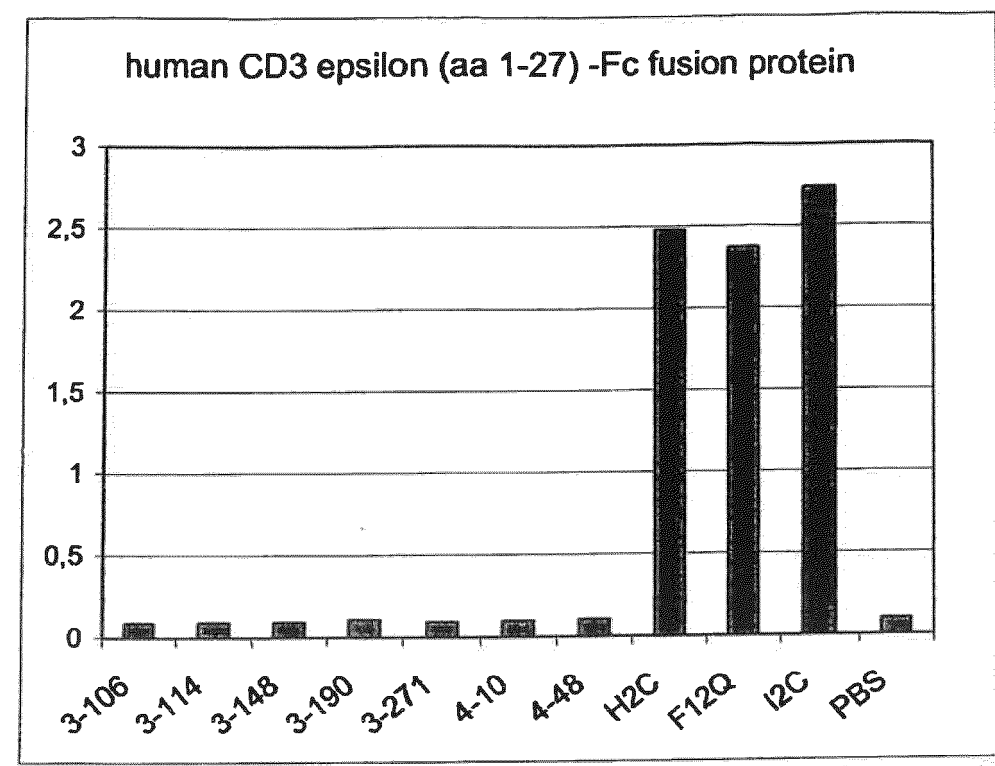
Figure 44

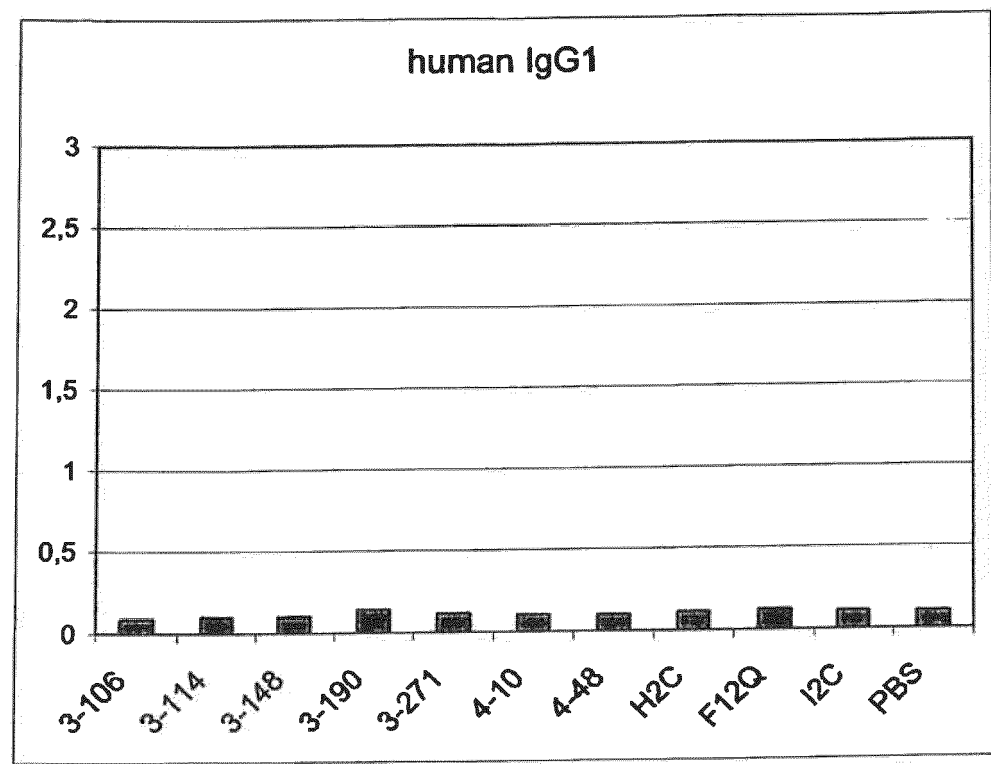
Figure 45

Figure 46 (1)

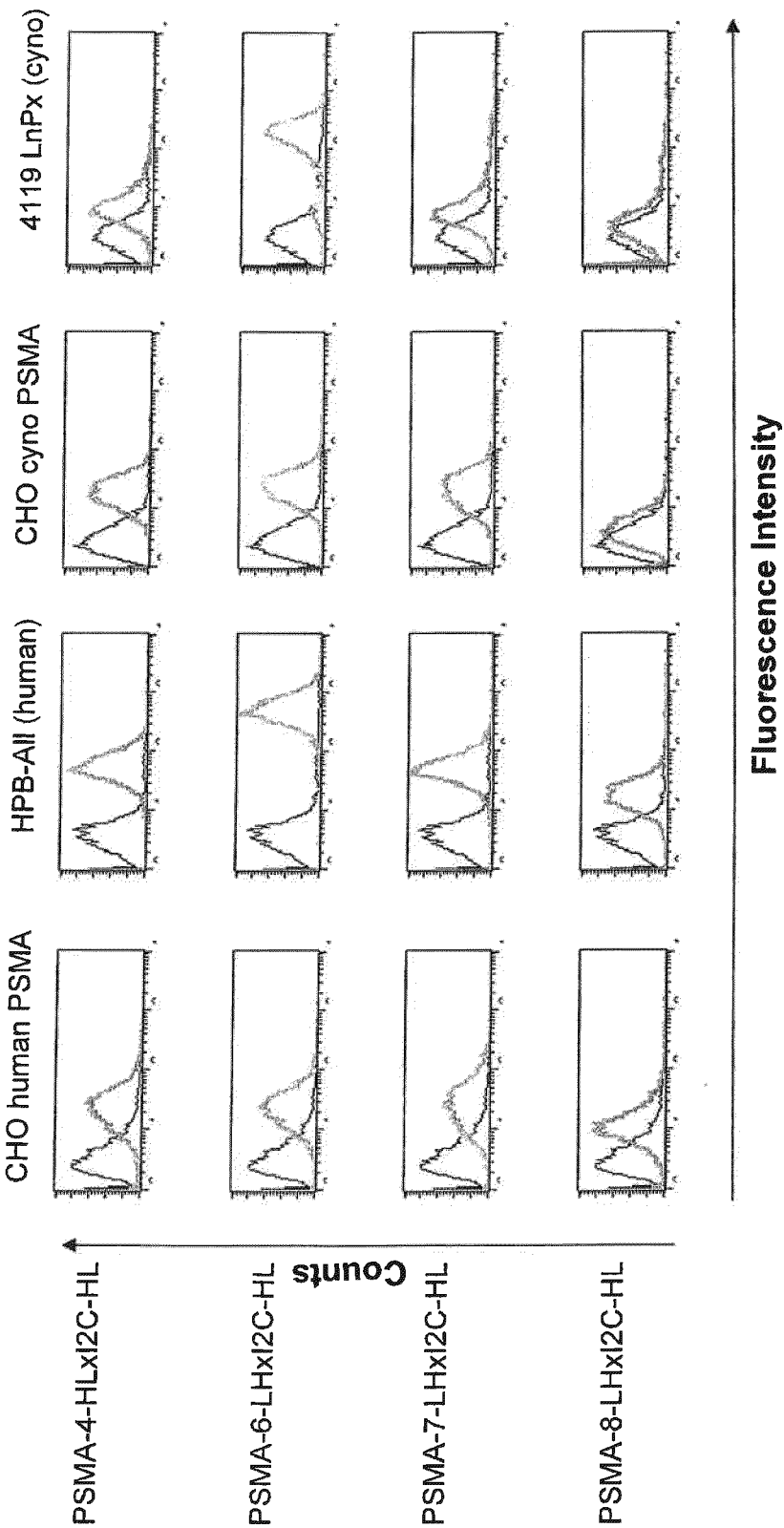


Figure 46 (2)

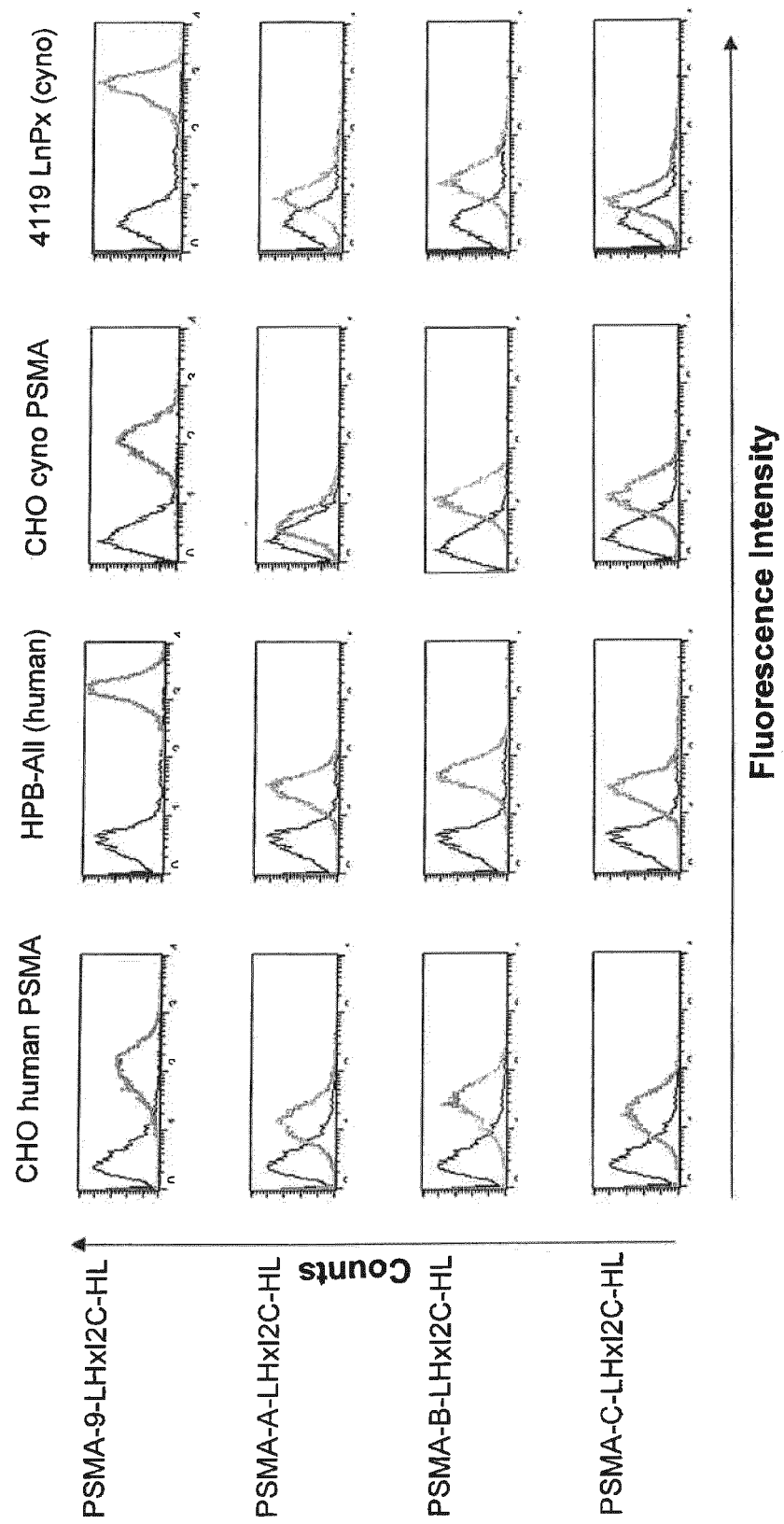


Figure 46 (3)

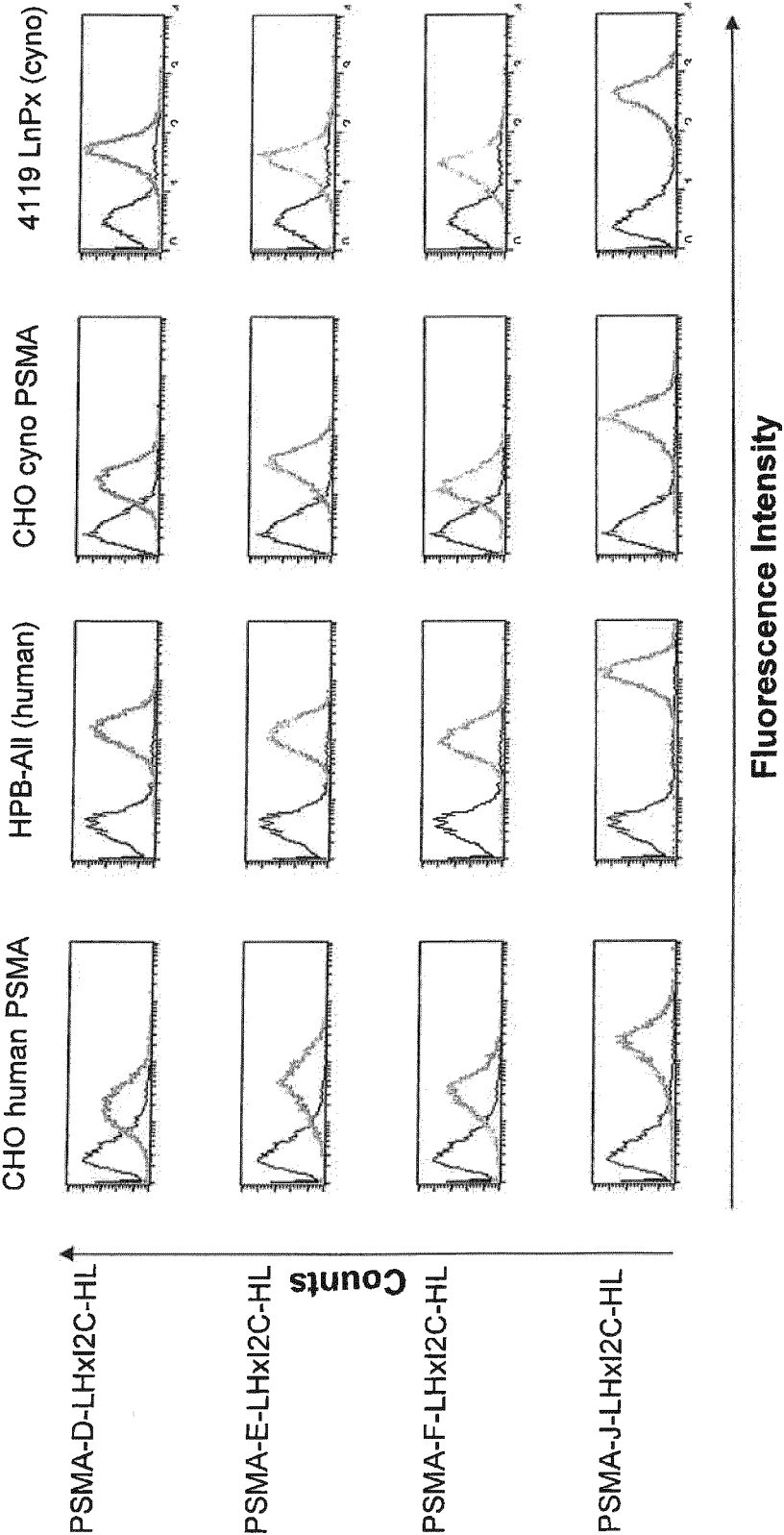


Figure 46 (4)

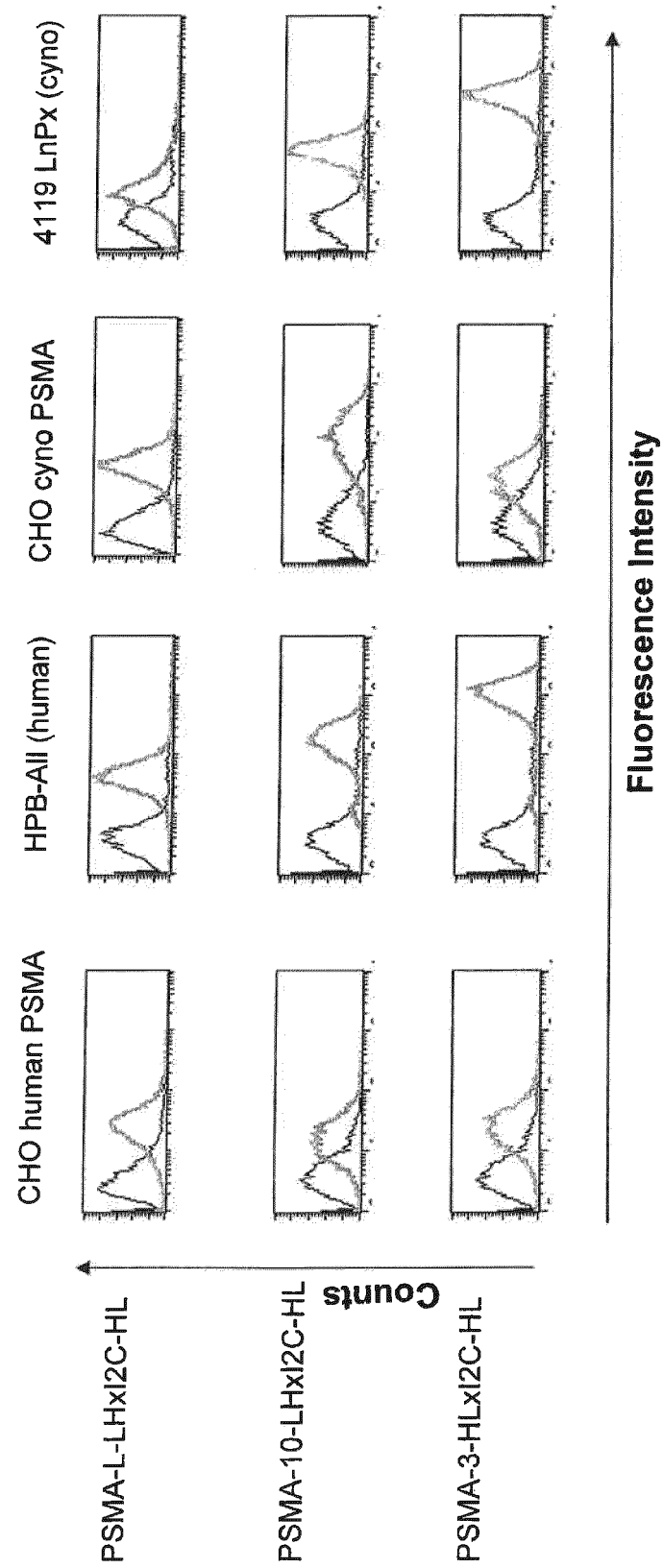
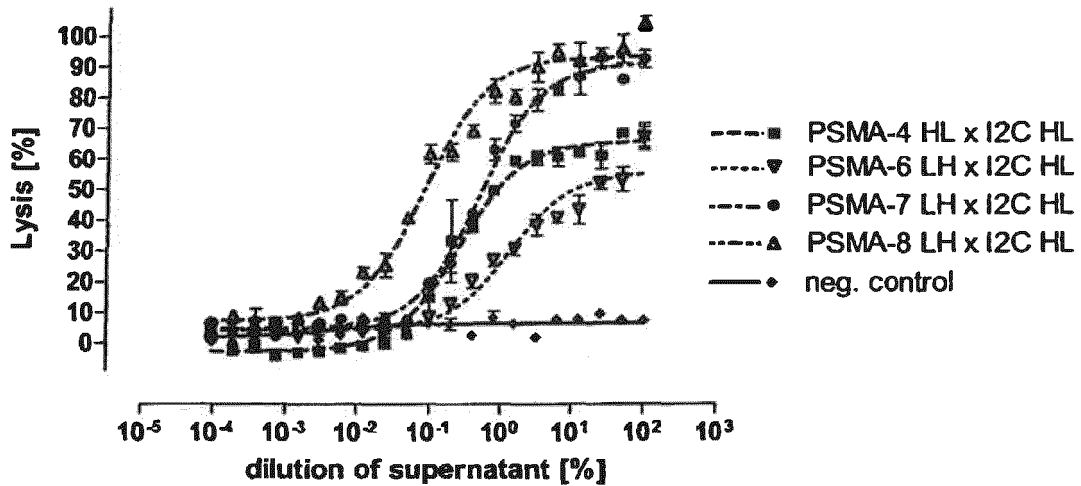


Figure 47(1)

- A) Effector cells: CD56 depleted unstimulated human PBMC
Target cells: CHO transfected with human PSMA



- B) Effector cells: CD56 depleted unstimulated human PBMC
Target cells: CHO transfected with human PSMA

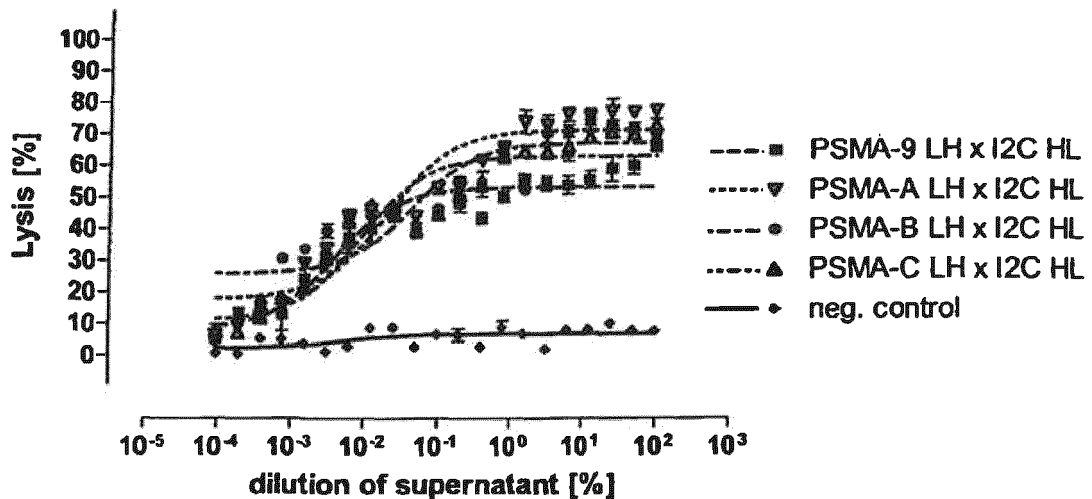
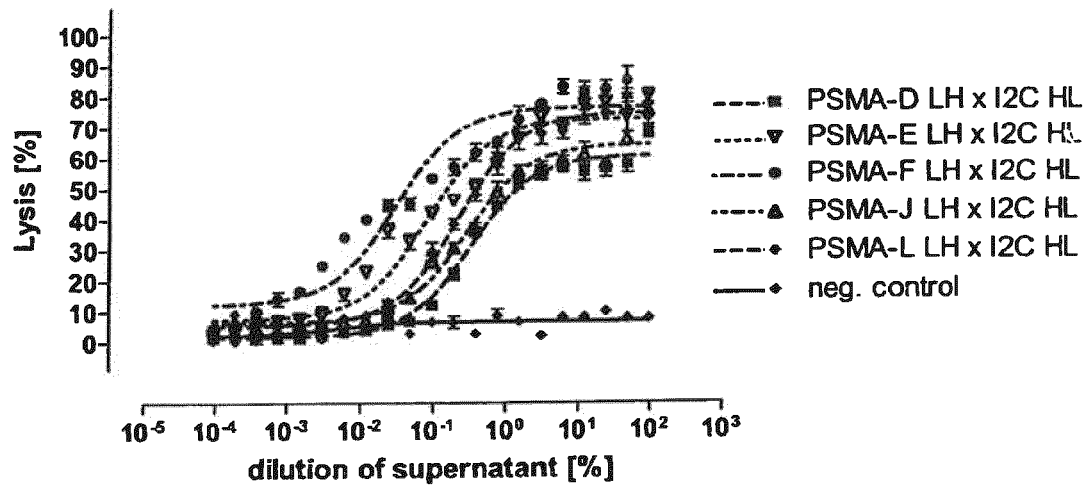


Figure 47(2)

- A) Effector cells: CD56 depleted unstimulated human PBMC
Target cells: CHO transfected with human PSMA



- B) Effector cells: CD56 depleted unstimulated human PBMC
Target cells: CHO transfected with human PSMA

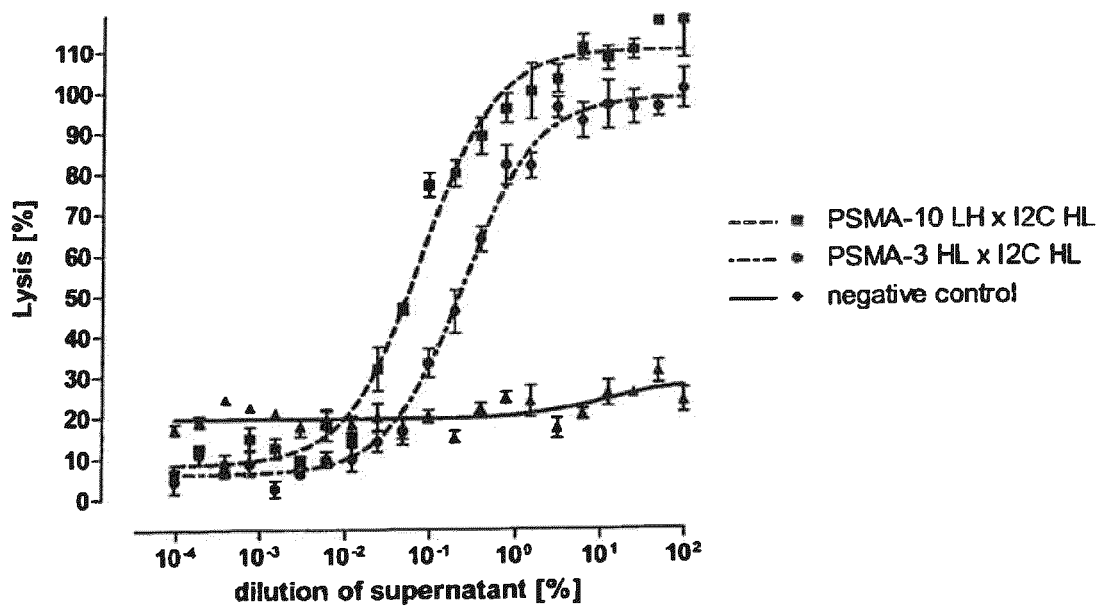
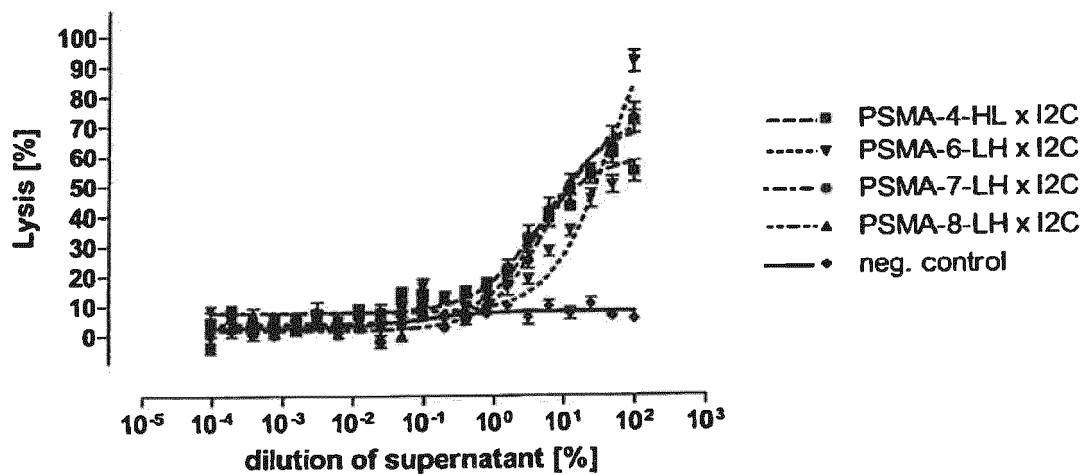


Figure 48(1)

- A) Effector cells: 4119LnPx
Target cells: CHO transfected with macaque PSMA



- B) Effector cells: 4119LnPx
Target cells: CHO transfected with macaque PSMA

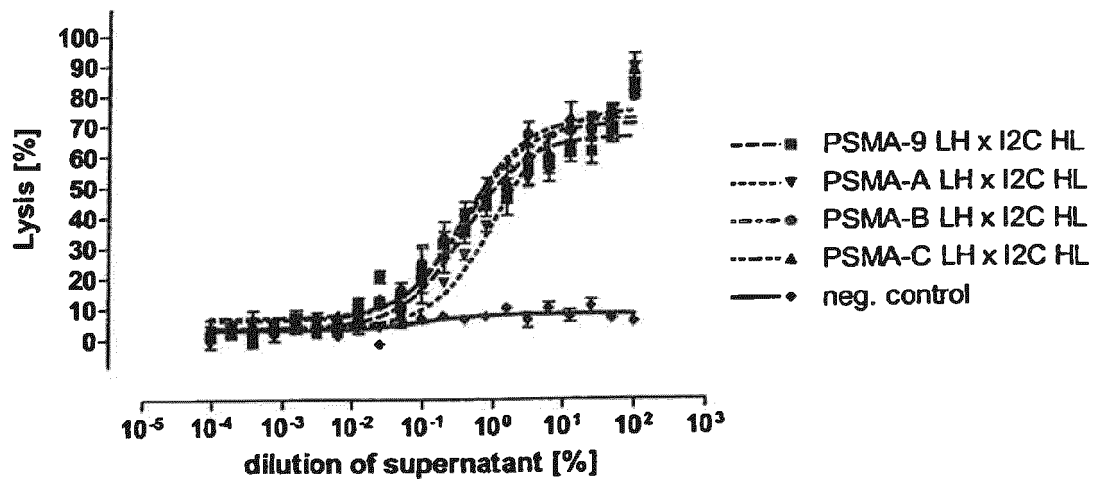
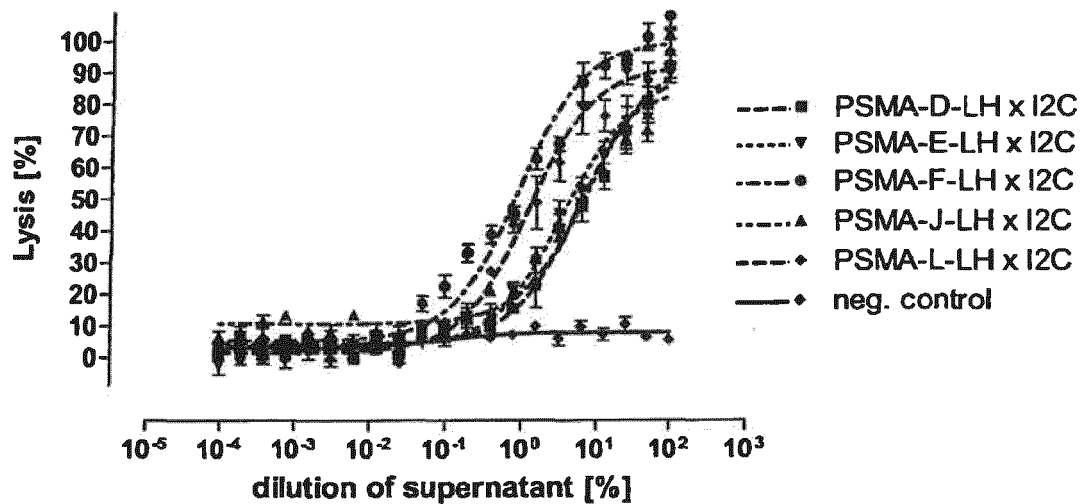


Figure 48(2)

A) Effector cells: 4119LnPx
Target cells: CHO transfected with macaque PSMA



B) Effector cells: 4119LnPx
Target cells: CHO transfected with macaque PSMA

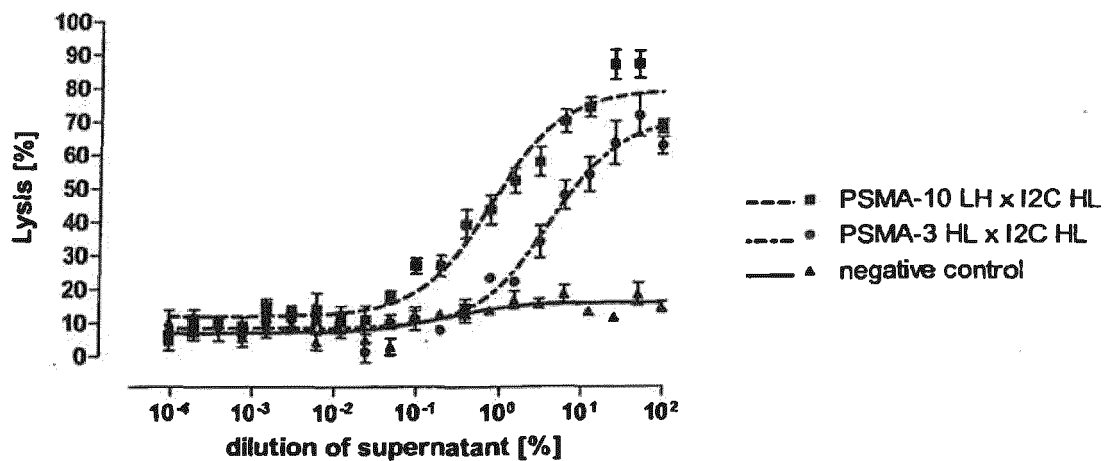


Figure 49a

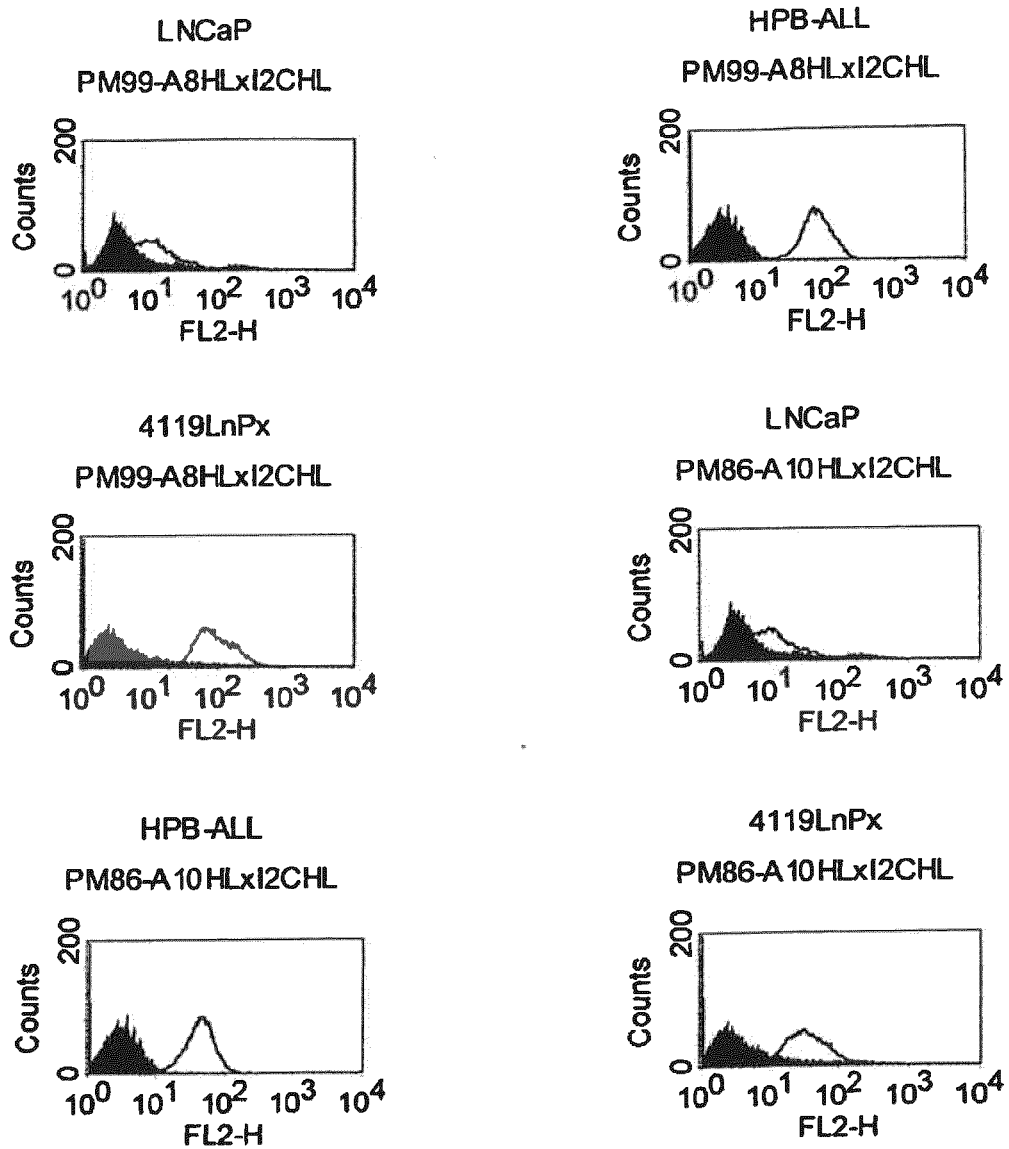


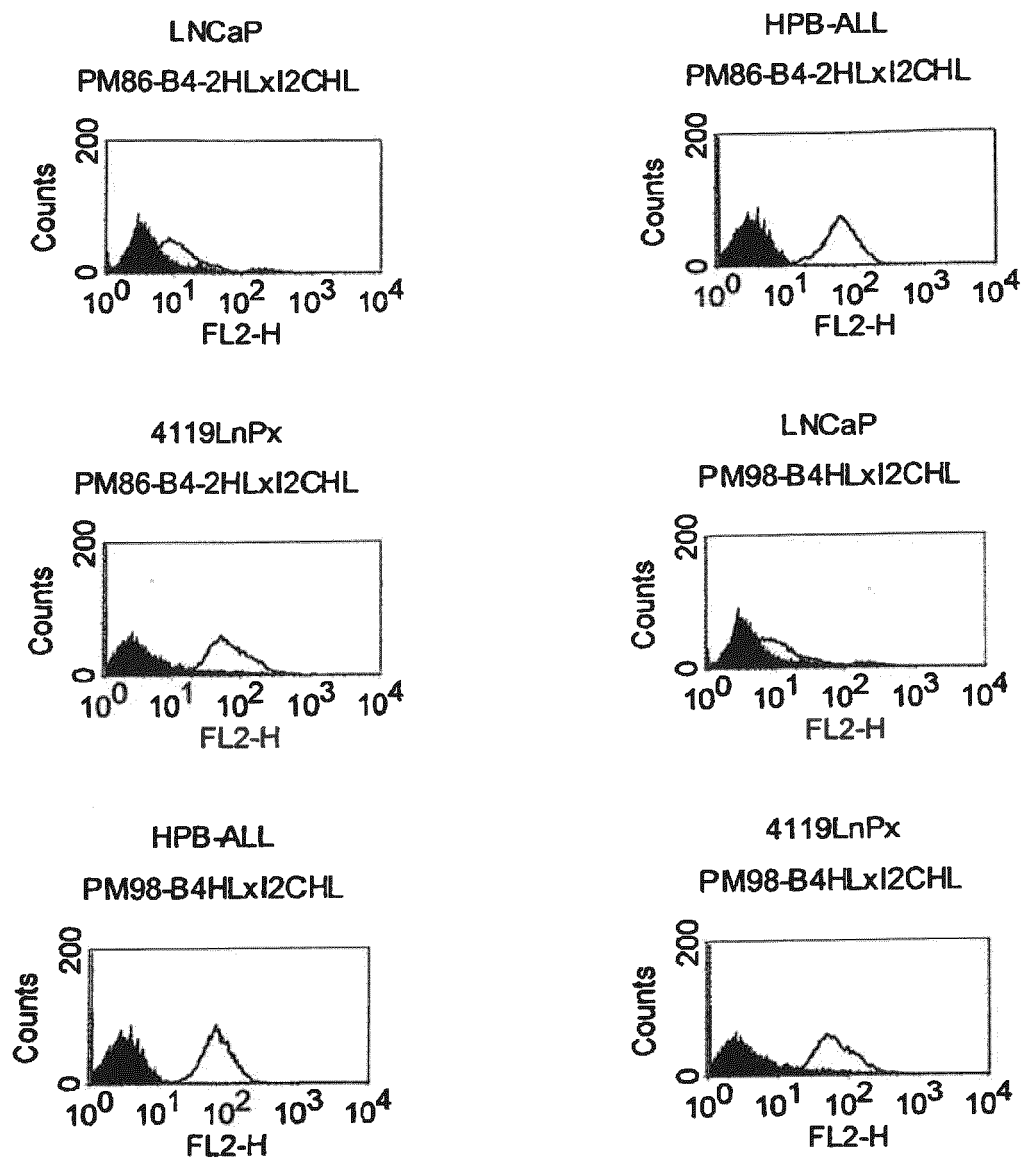
Figure 49b

Figure 49c

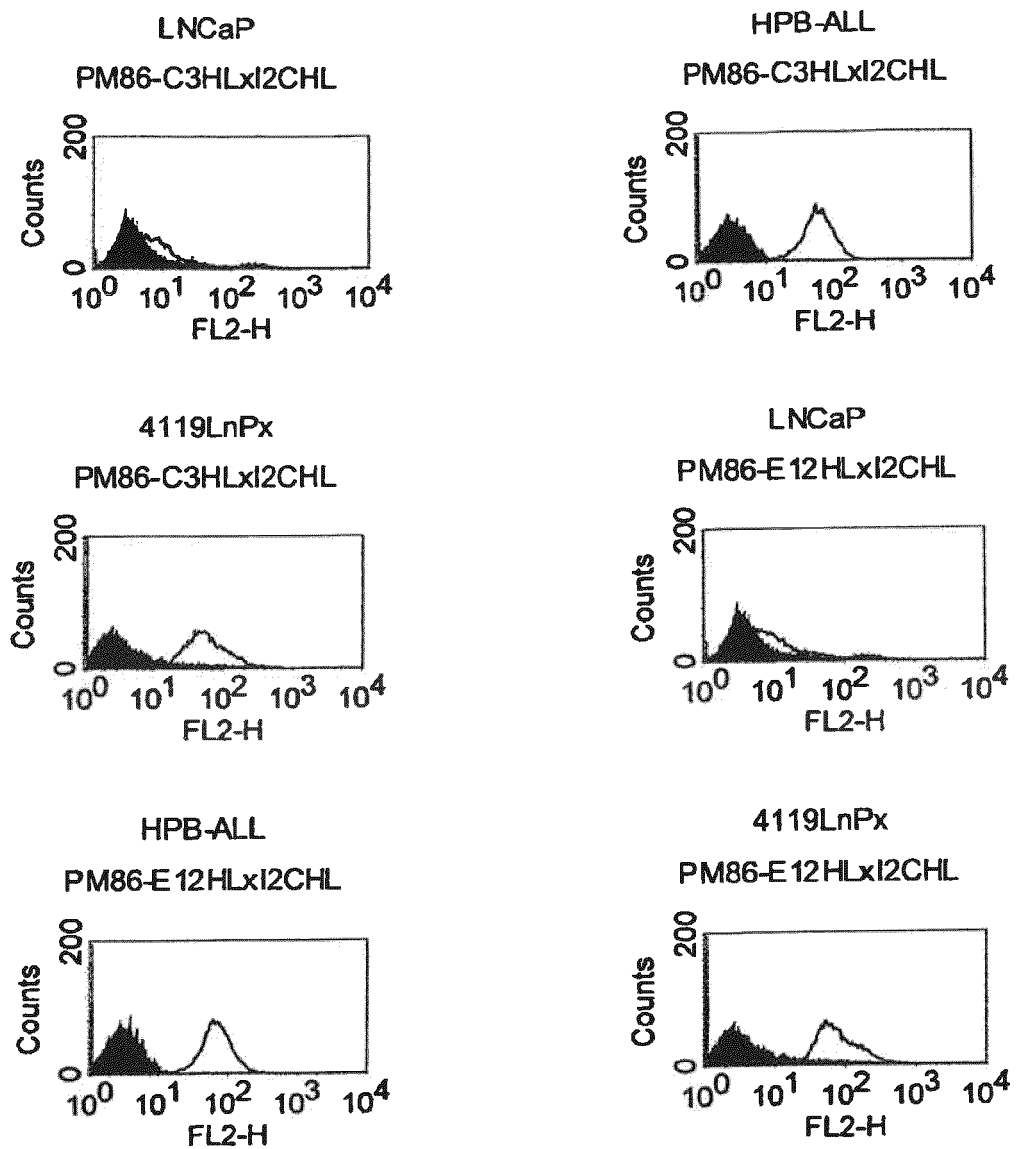


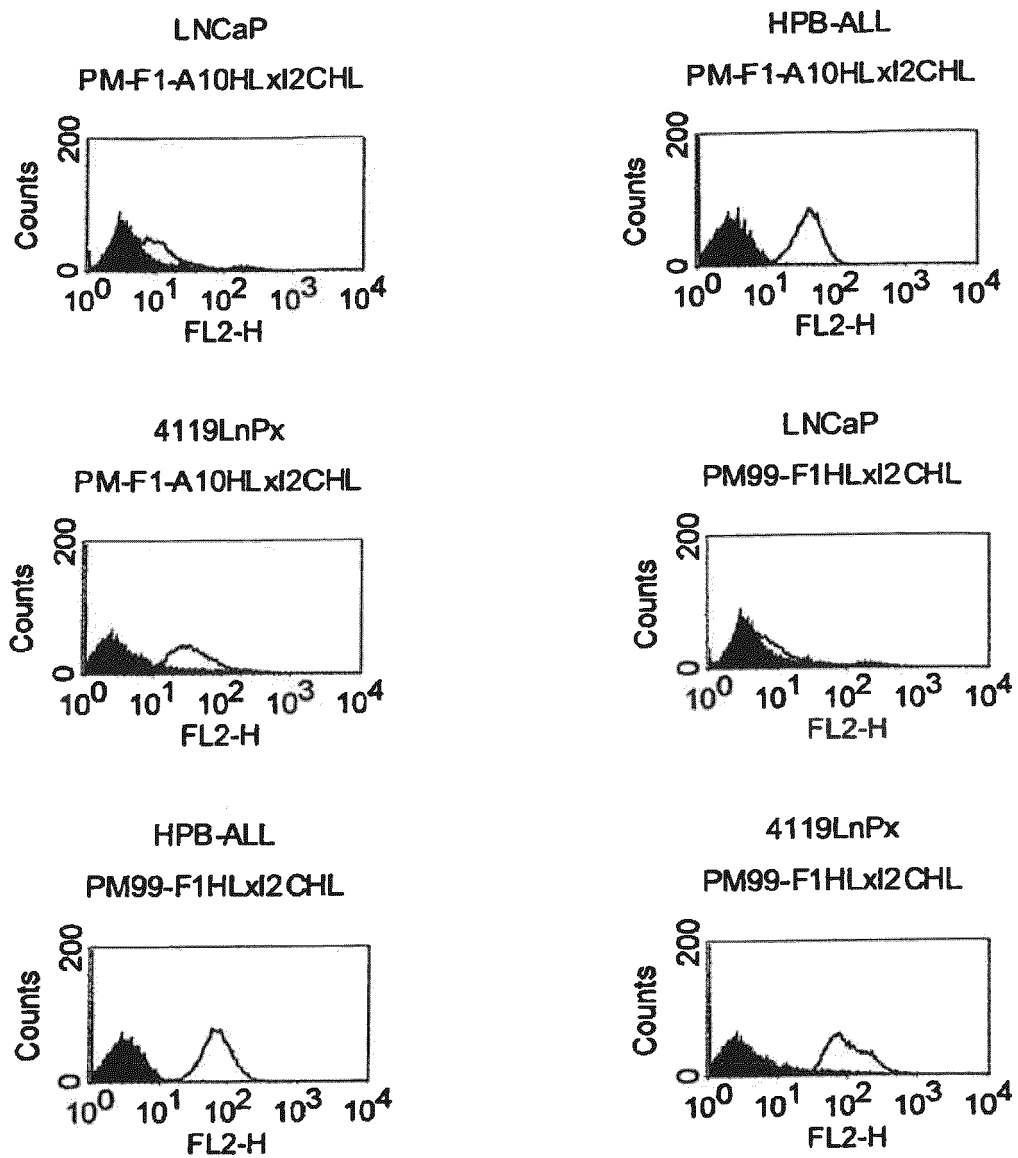
Figure 49d

Figure 49e

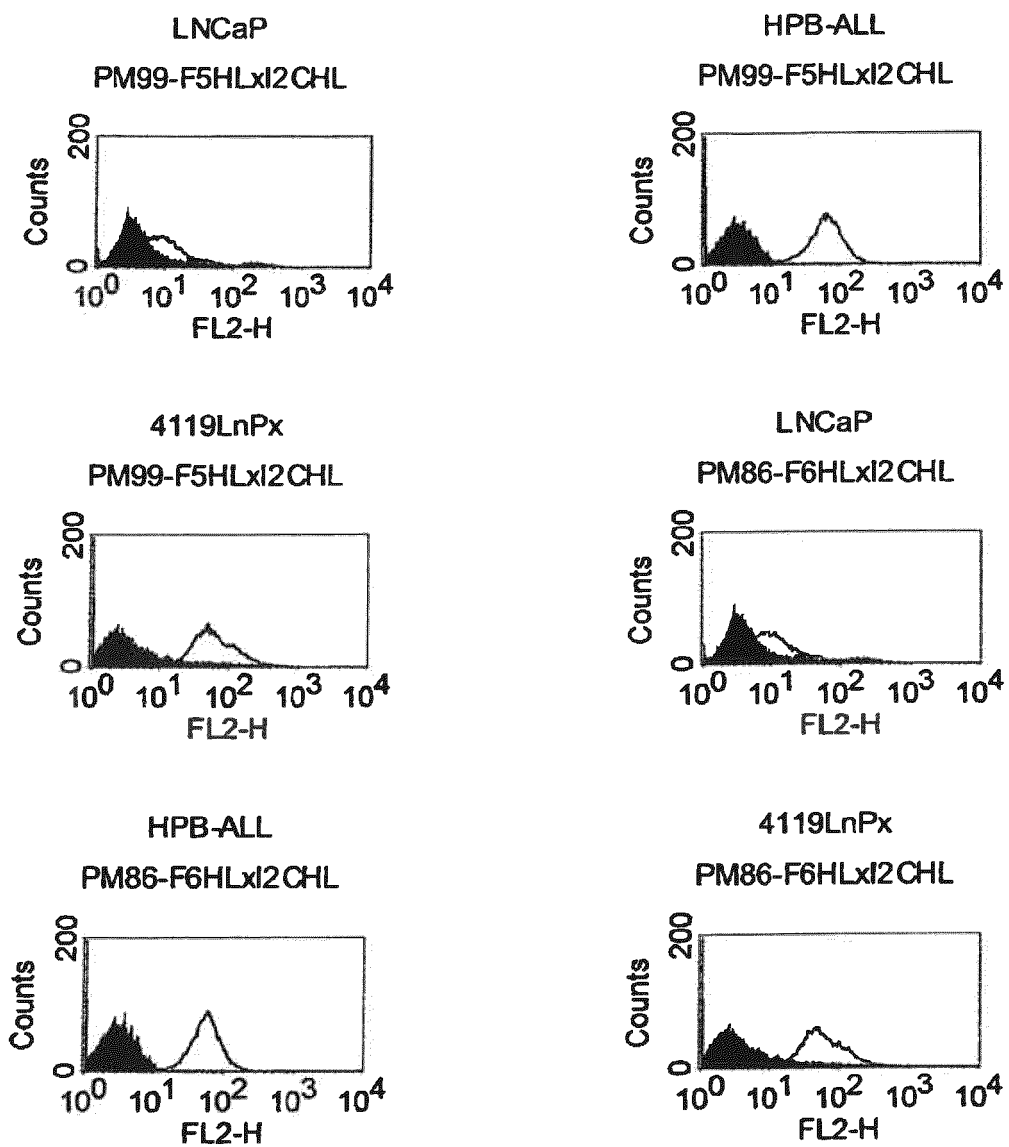
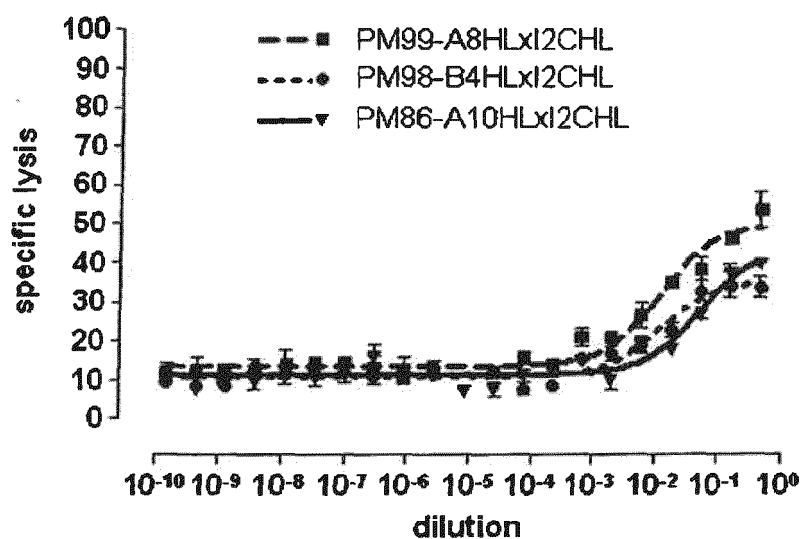


Figure 50(1)

Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: LNCaP



Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: LNCaP

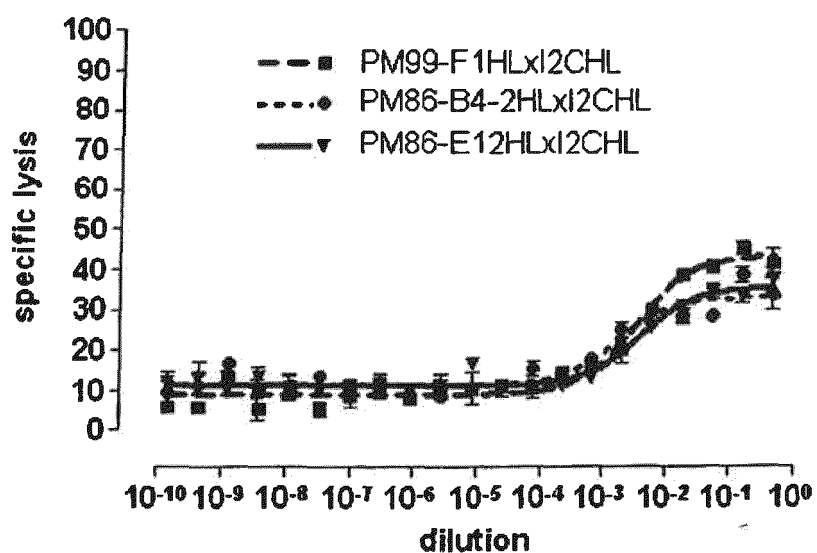
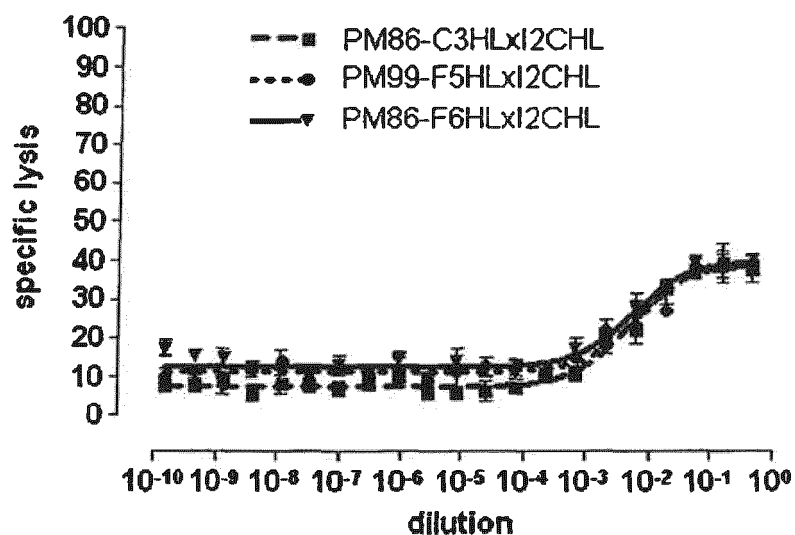


Figure 50(2)

Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: LNCaP



Effector cells: stimulated CD4/CD56 depleted human PBMC

Target cells: LNCaP

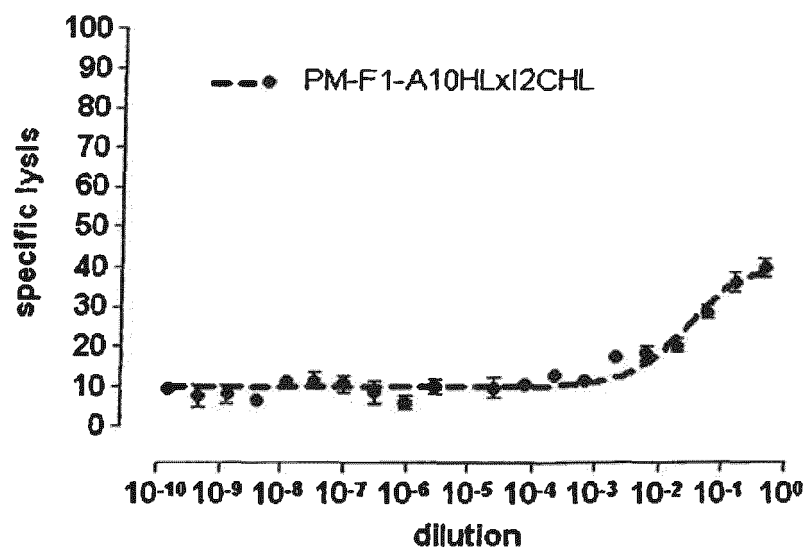
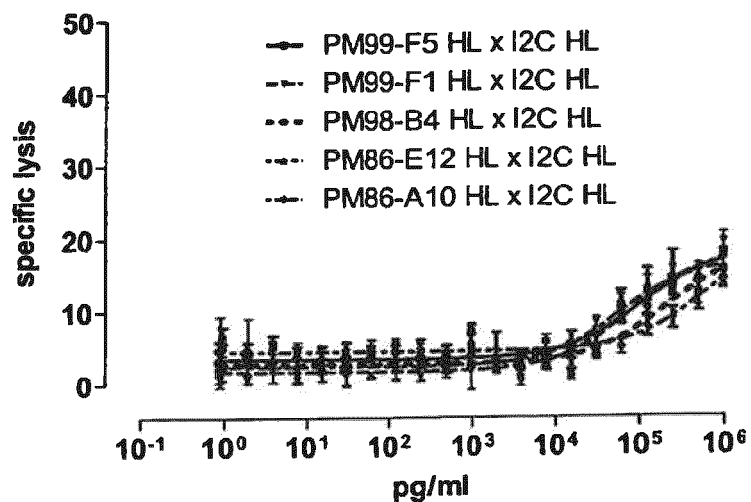


Figure 50(3)

A) Effector cells: 4119LnPx
Target cells: CHO transfected with macaque PSMA



B) Effector cells: 4119LnPx
Target cells: CHO transfected with macaque PSMA

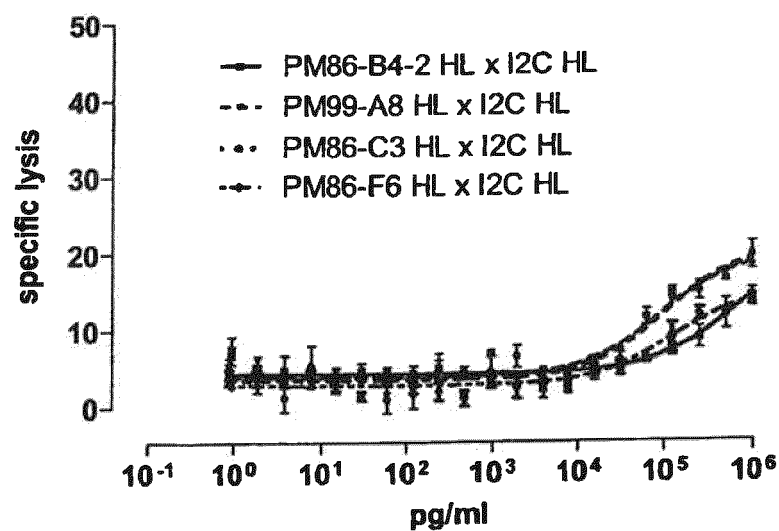


Figure: 51a

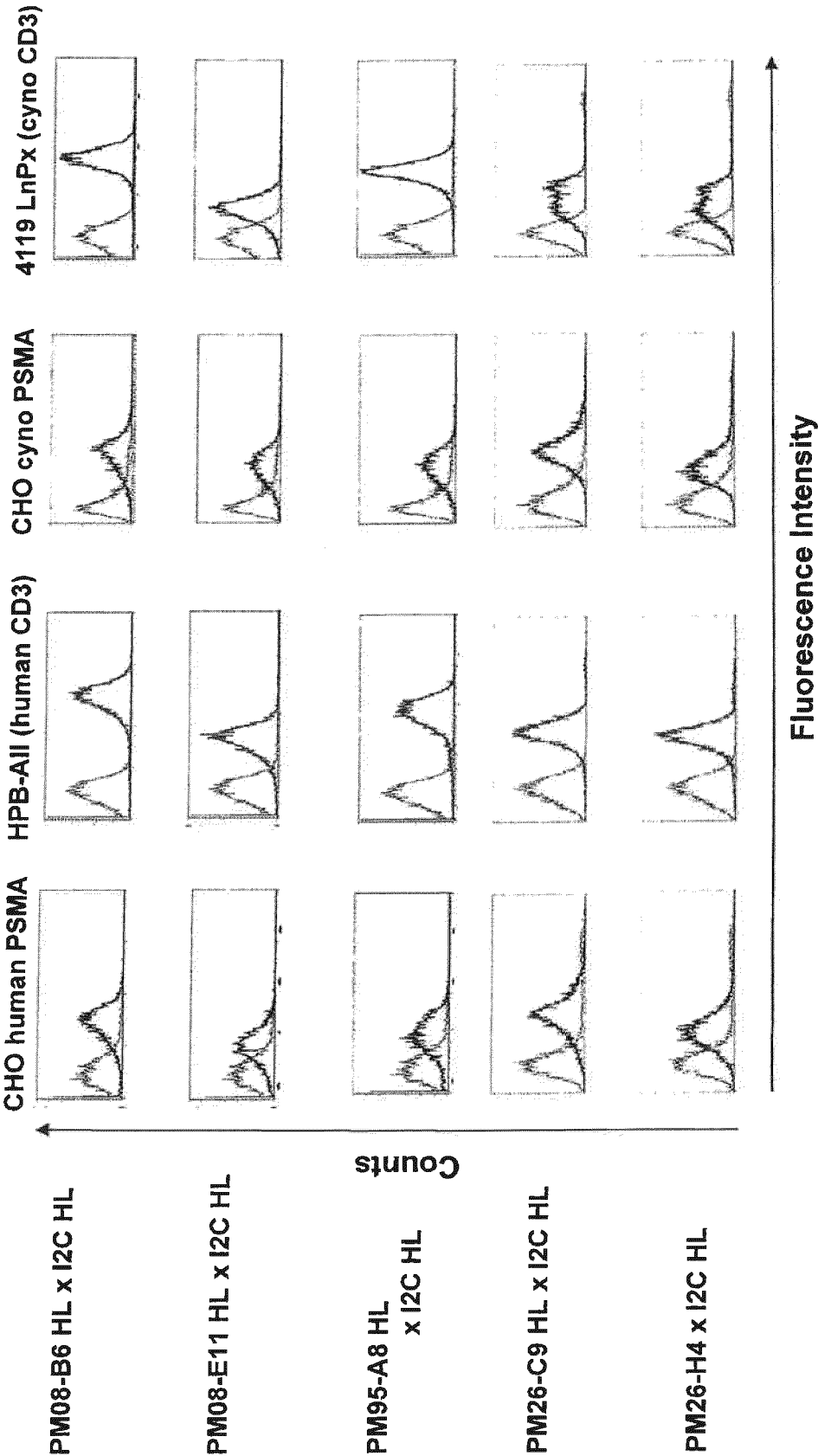


Figure: 51b

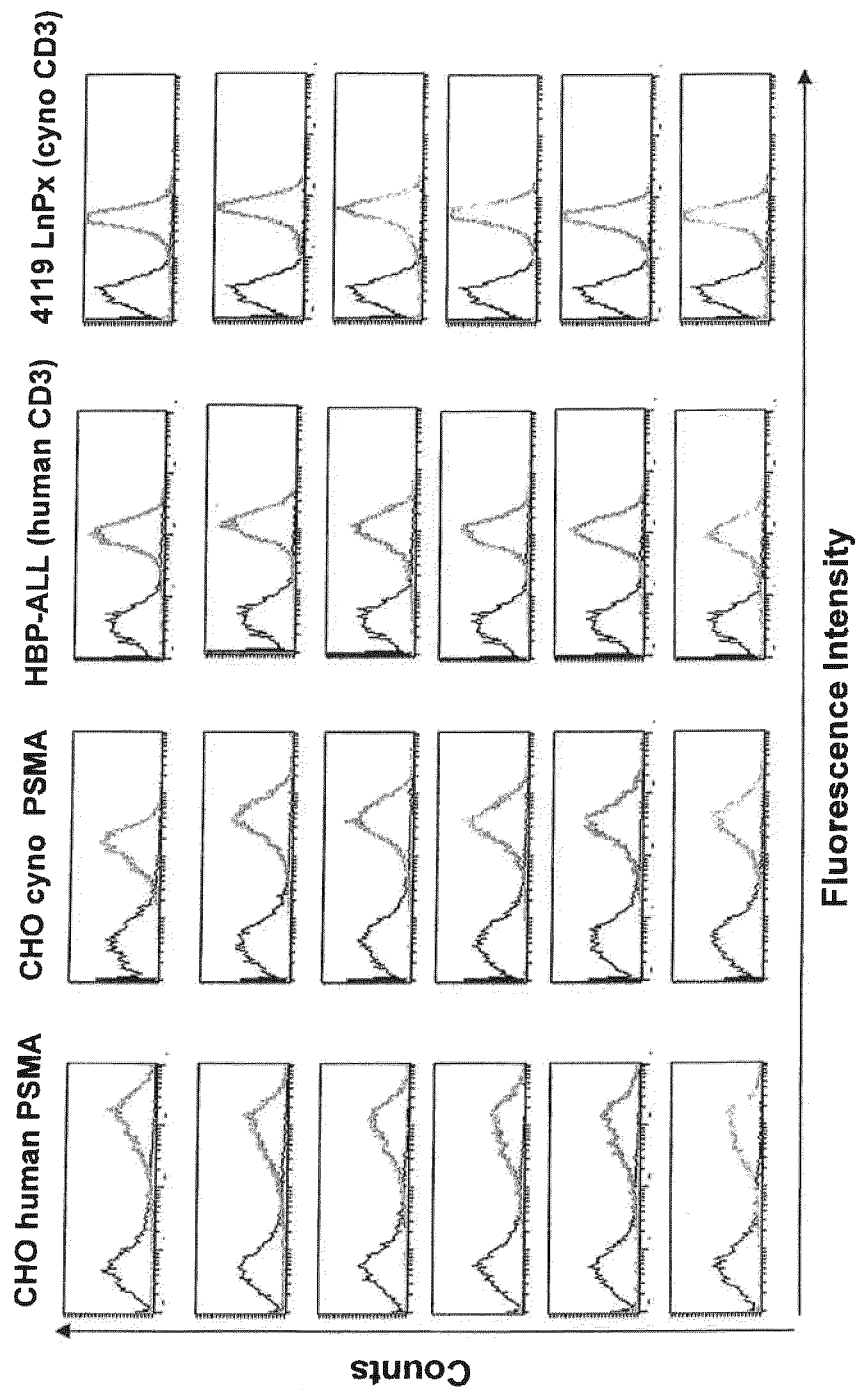


Figure: 51c

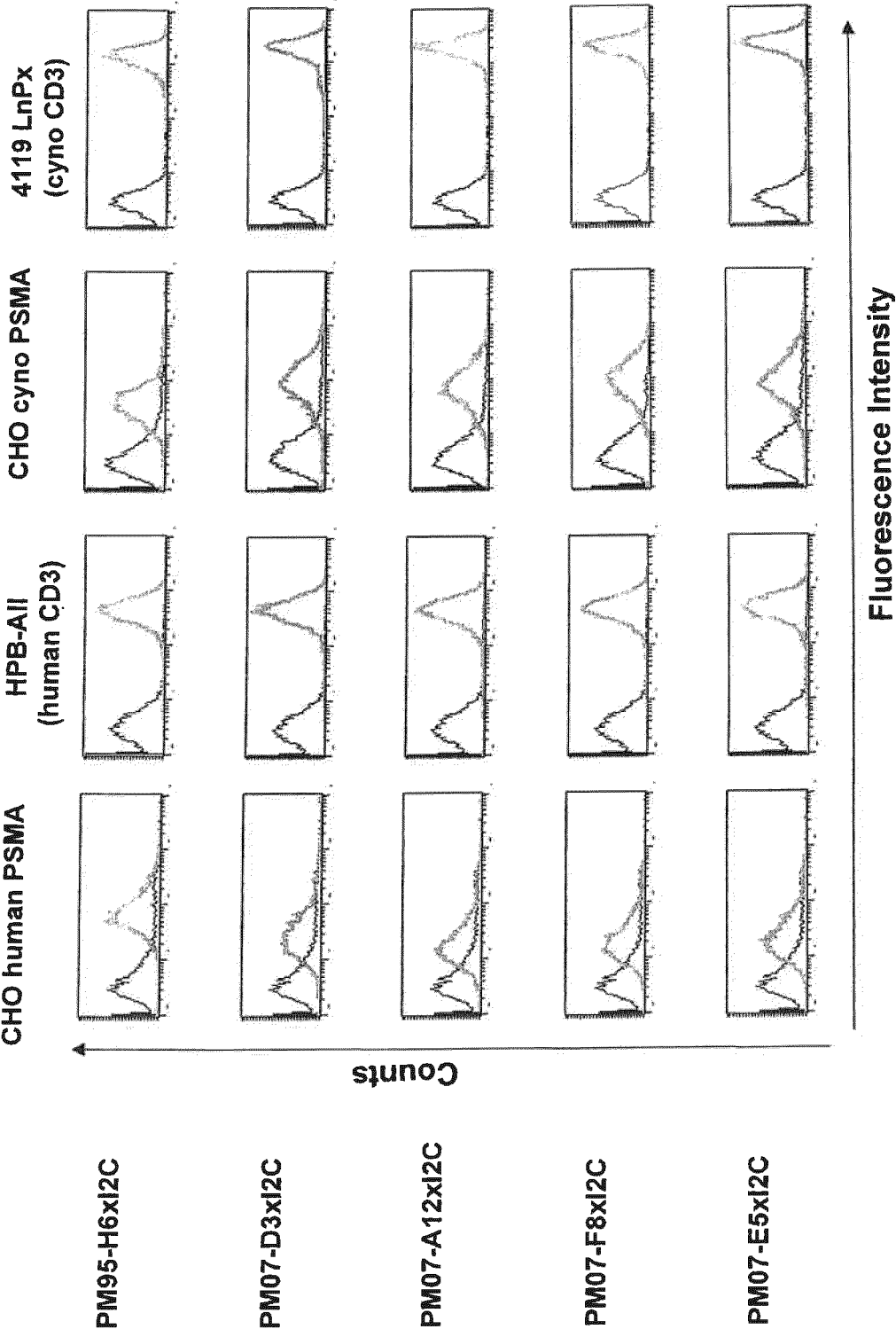
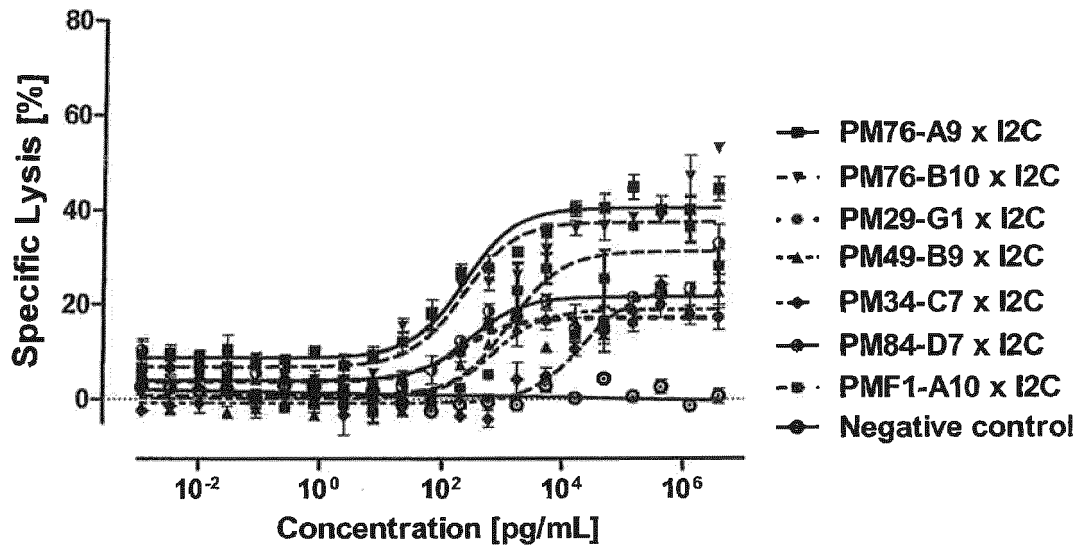
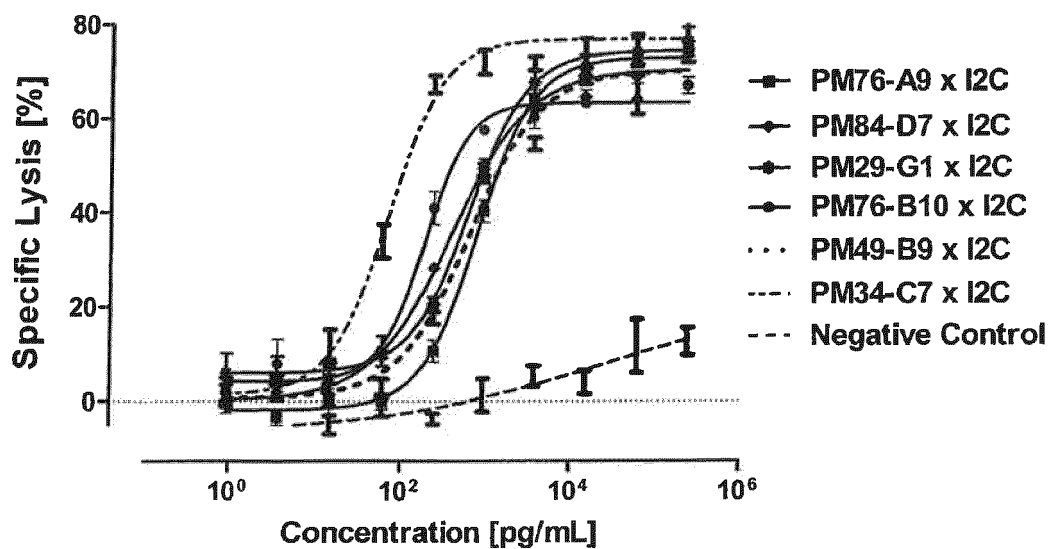


Figure 52

- A) Effector cells: 4119LnPx
Target cells: CHO transfected with macaque PSMA



- B) Effector cells: human unstimulated PBMC
Target cells: CHO transfected with human PSMA



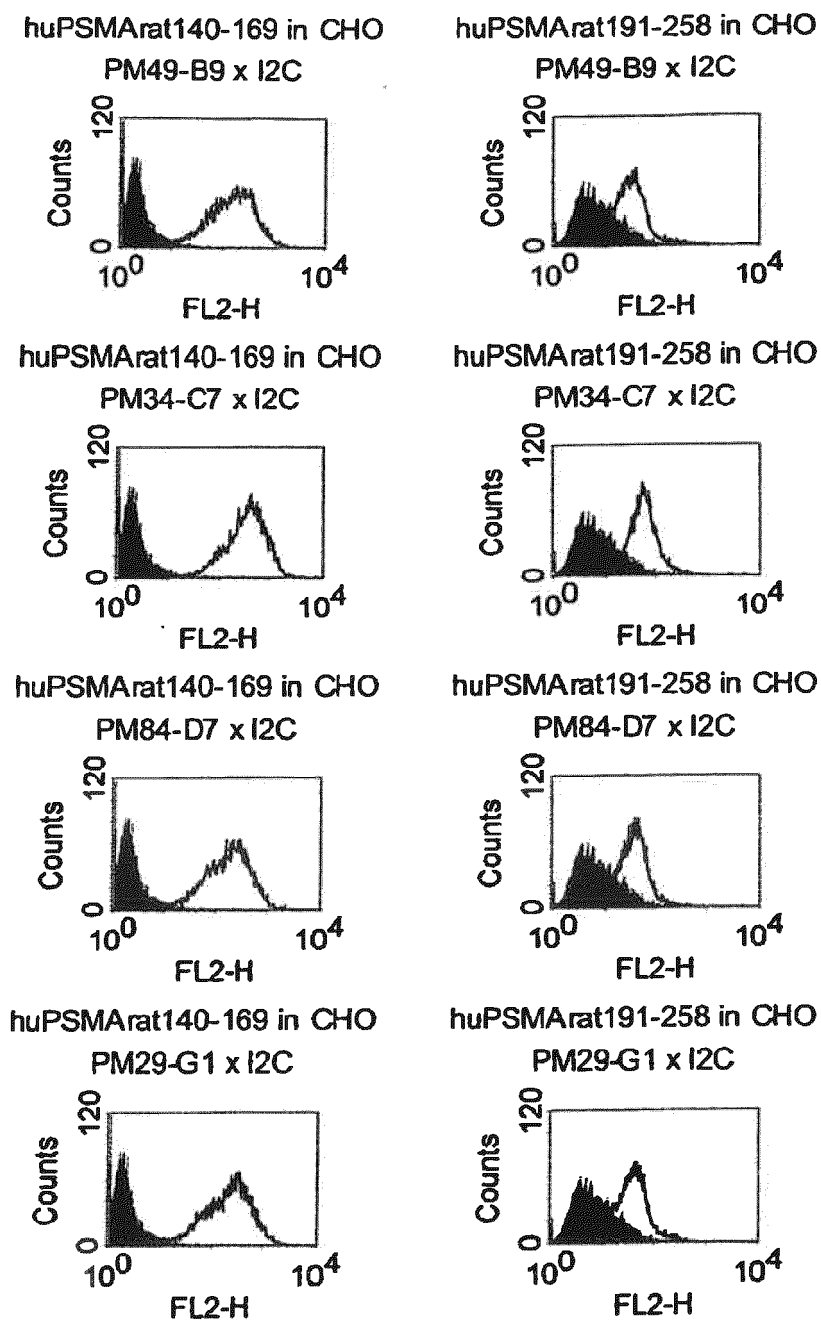


Figure 53a

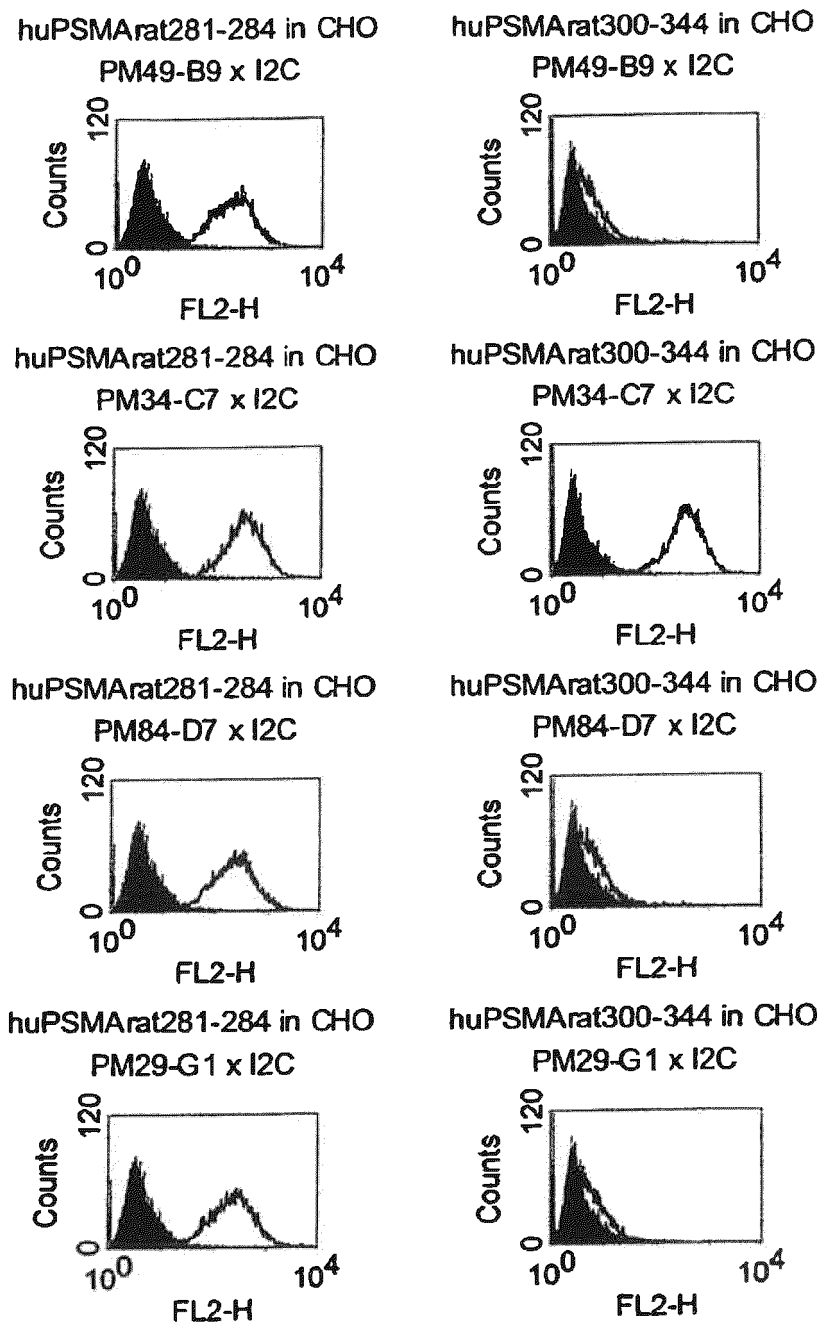


Figure 53b

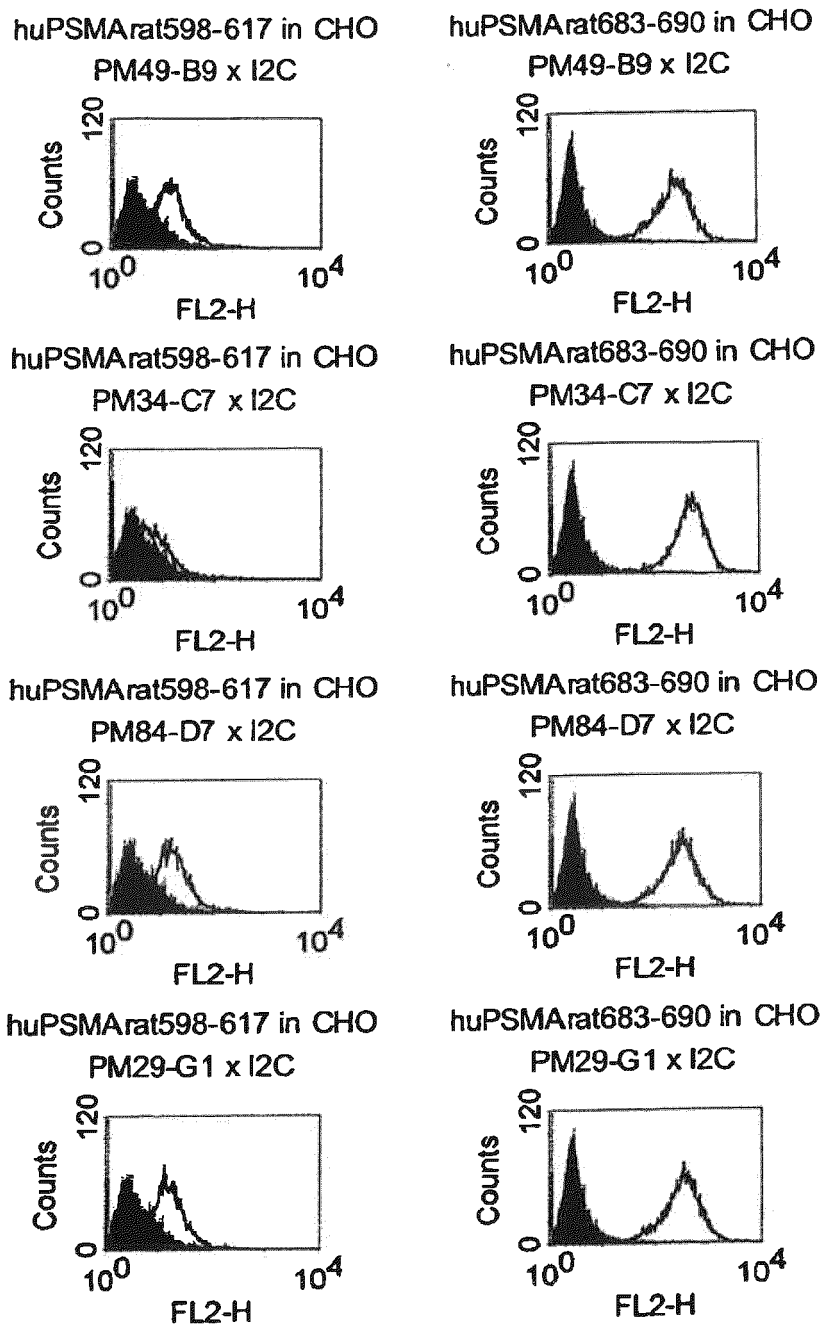
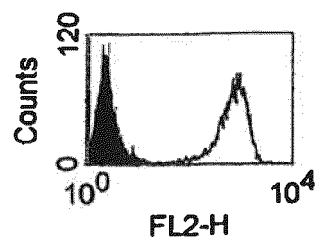


Figure 53c

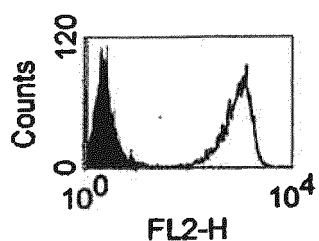
huPSMArat716-750 in CHO

PM49-B9 x I2C



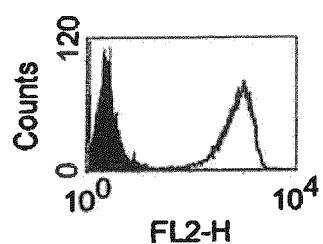
huPSMArat716-750 in CHO

PM34-C7 x I2C



huPSMArat716-750 in CHO

PM84-D7 x I2C



huPSMArat716-750 in CHO

PM29-G1 x I2C

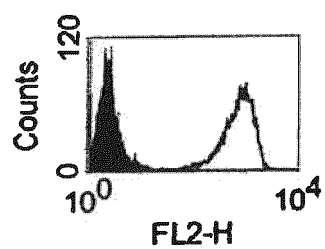


Figure 53d

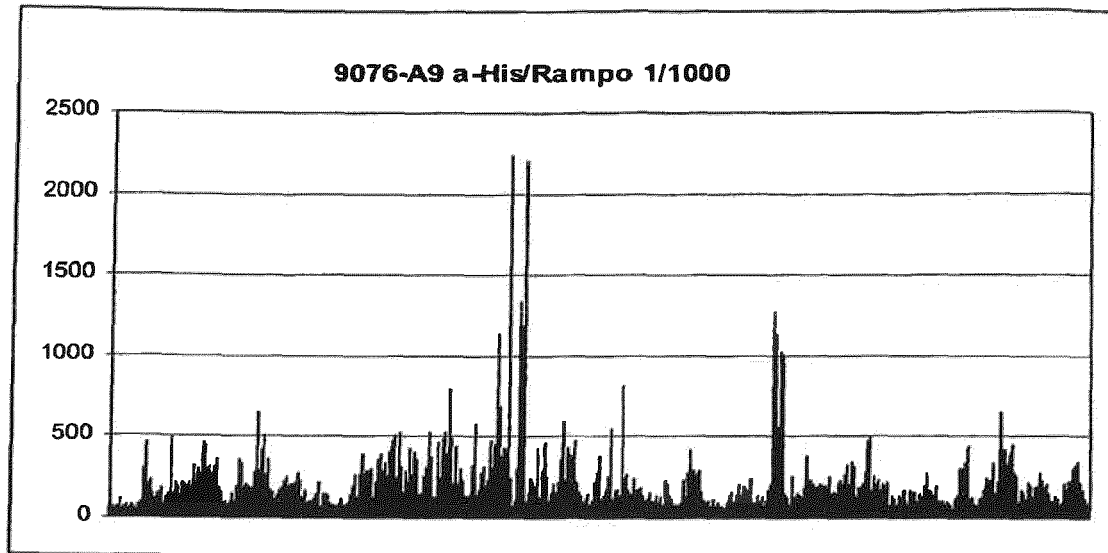


Figure 54

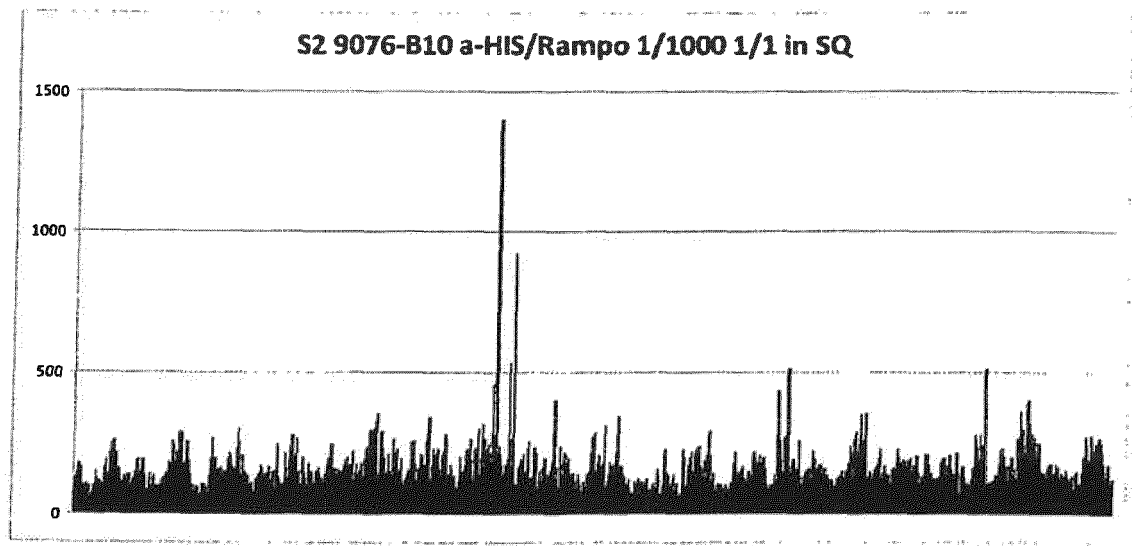


Figure 55

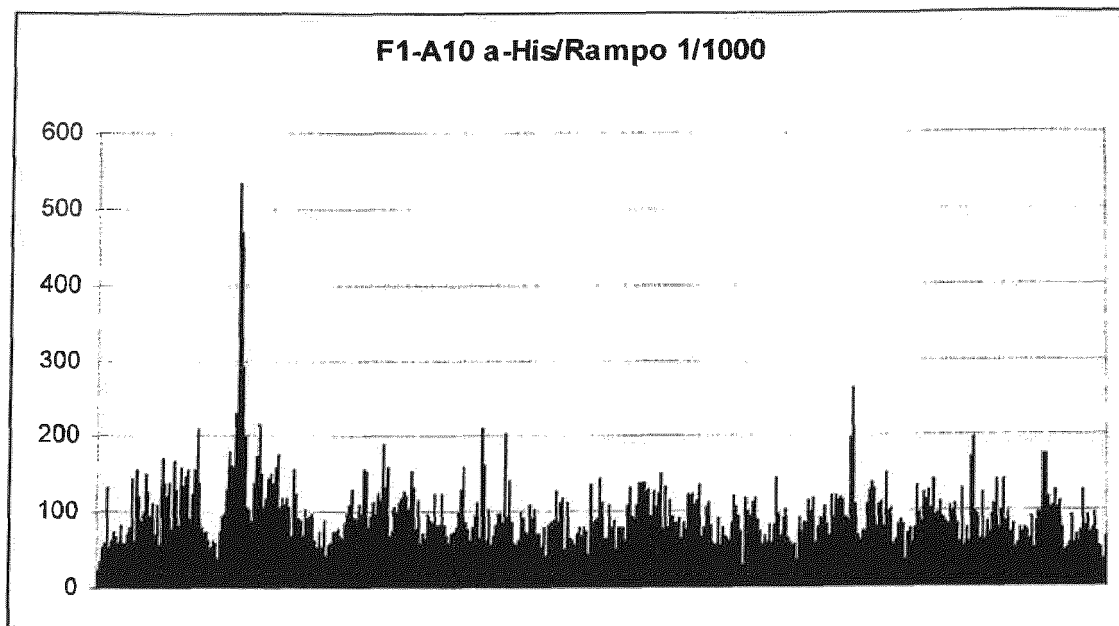


Figure 56

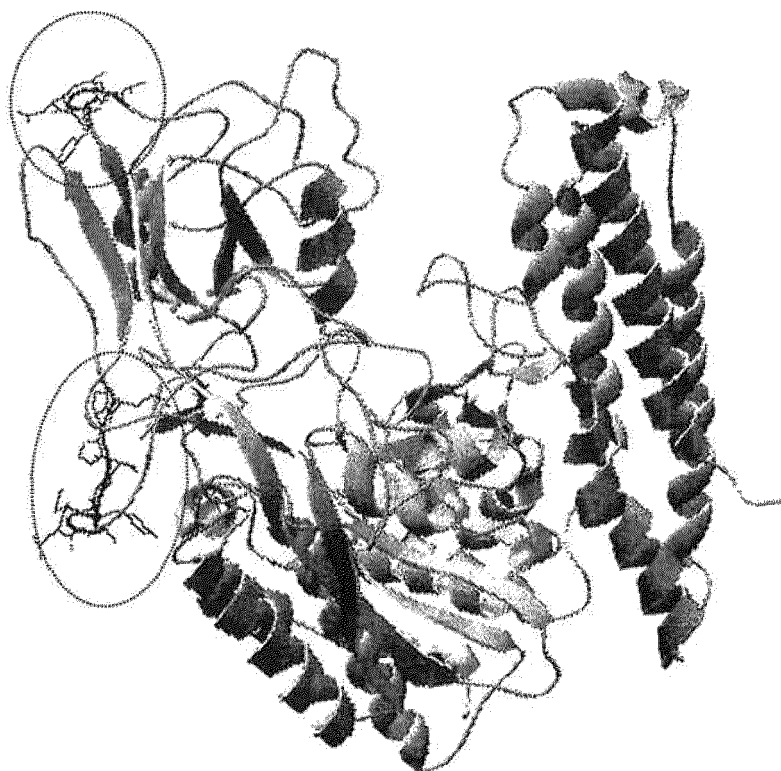
Figure 57

MP 9076-A9
MP 9076-B10

GLY332	v	■
PHE333	v	■
THR334 v v	v	■
GLY335 v v	v	■
ASN336 v v	v	■
PHE337 v v	v	■
SER338 v v	v	■
THR339 v v	v	■
GLN340	v	■
s LYS341	v	■

F1-A10

PHE144	v	■
GLU145 v v	v	■
PRO146 v v	v	■
PRO147 v v	v	■
PRO148 v v	v	■
PRO149 v v	v	■
GLY150 v v	v	■
TYR151 v v	v	■
GLU152 v v	v	■
ASN153 v v	v	■
VAL154 v v	v	■
SER155	v	■





EUROPEAN SEARCH REPORT

Application Number

EP 22 17 8586

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EPO FORM 1503 03.82 (P04C01)

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
A	WO 2007/042261 A2 (MICROMET AG [DE]; KISCHEL ROMAN [DE]; RAUM TOBIAS [DE]; SCHLERETH BERN) 19 April 2007 (2007-04-19) * claims; examples *	1-15	INV. C07K16/28 C07K16/22 C07K16/30 C07K16/40 A61K39/00
A	WO 2006/089230 A2 (MEDAREX INC [US]; HUANG HAICHUN [US] ET AL.) 24 August 2006 (2006-08-24) * the whole document *	1-15	
A	WO 2004/106381 A1 (MICROMET AG [DE]; KUFER PETER [DE]; LUTTERBUESE RALF [DE]; KOHLEISEN B) 9 December 2004 (2004-12-09) * page 11, line 24 - page 12, line 29 * * claims * * examples *	1-15	
A	BÜHLER P ET AL: "A bispecific diabody directed against prostate-specific membrane antigen and CD3 induces T-cell mediated lysis of prostate cancer cells", CANCER IMMUNOLOGY, IMMUNOTHERAPY, SPRINGER, BERLIN, DE, vol. 57, no. 1, 20 June 2007 (2007-06-20), pages 43-52, XP019561052, ISSN: 1432-0851, DOI: 10.1007/S00262-007-0348-6 * the whole document * * in particular: * * abstract *	1-15	TECHNICAL FIELDS SEARCHED (IPC) C07K
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 10 February 2023	Examiner Tuynman, Antonin
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EUROPEAN SEARCH REPORT

Application Number

EP 22 17 8586

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